

Skill versus Strength in Swallowing Training: Neurophysiological, Biomechanical, and Structural Assessments

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Oshrat Sella

Department of Communication Disorders

The University of Canterbury, Christchurch, New Zealand

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Dedicated to my beloved grandparents, Teresa and Shlomo Schneider,
who survived the holocaust and found strength to restart their lives.

Abstract

Swallowing is a complex sensorimotor behaviour that includes precisely-timed bilateral activation and relaxation of muscles of the face, lips, tongue, cheeks, palate, larynx, pharynx and oesophagus. These events of activation and inhibition are controlled by many structures of the brain and are executed by cranial nerves that carry motor and sensory information to and from the swallowing muscles.

Swallowing disorders are common sequelae of many neurological and structural disorders, including stroke, Parkinson's disease, and head and neck cancer. Changes to swallowing physiology are also prevalent in older individuals, but these changes do not necessarily translate to dysphagia. Decreased muscle strength, changes to motor unit properties, and hypotrophic changes in skeletal muscles can result in age-related changes in swallowing physiology. In addition to muscular changes, neural changes might also change swallowing function in older subjects.

The motor-learning literature presents a clear distinction between the differential applications and effects of skill- and strength-training approaches for rehabilitation of limb movement. In contrast to limb-movement rehabilitation, swallowing rehabilitation approaches consist mainly of strength training, although the pathophysiological basis for dysphagia is not always weakness. Therefore, this Phase I clinical-trial critically evaluated a unique swallowing skill training protocol in which the goal of intervention is to increase precision of motor control during swallowing. A Phase I clinical-trial was necessary to identify the appropriate protocol for inducing neurophysiological, biomechanical, and structural adaptations, to estimate effect sizes, and to identify adverse effects.

The first and primary question addressed in this thesis was whether swallowing skill training would produce greater physiological effects in healthy subjects than a traditional swallowing strength training approach. In order to answer this question, three levels of assessment were included. *Neurophysiological assessment* consisted of delivering single-pulse transcranial magnetic stimulation (TMS) over the M1 area that sends efferent projections to the submental muscle group during a functional task of volitional saliva swallowing, and during a non-functional task of submental muscle group contraction. *Biomechanical assessments* consisted of pharyngeal and upper esophageal sphincter (UES) pressure measurements using pharyngeal manometry during effortful and non-effortful swallowing tasks, submental muscle activation measurements using surface electromyography (sEMG) during effortful and non-effortful swallowing tasks, and hyoid displacement using ultrasonography. *Structural assessment* consisted of measuring the

cross sectional area of the submental muscle group. Finally, motor performance during training, and subjective ratings of the training protocols were assessed. Two skill training protocols were developed to assess the use of immediate versus delayed visual feedback in swallowing skill training. In addition, a pilot study aimed at examining the effects of increased dosage of training sessions was conducted.

Forty healthy subjects (20 young, and 20 old; 20 females and 20 males) were allocated to skill and strength training groups in a counterbalanced manner. Strength training consisted of execution of the effortful swallowing technique targeting increased demand for strength. Skill training targeted precise timing and force execution during swallowing execution. Several motor-learning principles were considered in devising the training protocols, including the principles of task specificity and high intensity of training. Biofeedback was included to promote motor learning. Since the submental muscle group plays an important role in hyolaryngeal excursion, the current study utilized submental sEMG biofeedback using custom-made training software. The training protocols consisted of 1000 repetition of swallowing over a 2-week period. Subjects trained for an hour, five days a week, for 2 weeks (i.e., 10 training sessions). The extended dosage protocol included 10 subjects and comprised an additional eight sessions.

The results indicated that there was a significant difference in submental activation following training, with strength training having an increase in sEMG peak amplitude in comparison to skill training. There were no other differences between groups at the 5% error level. Patterns of change were revealed when marginally significant results ($0.05 < p \leq 0.10$) were investigated as well. Strength training resulted in a trend towards increased neural drive for volitional effortful-type tasks (i.e., effortful saliva swallowing, effortful water swallowing, and submental muscle contraction) as indicated by increased MEP magnitude ($p = 0.07$) which was consistent with significantly increased peak amplitude of submental activity measures ($p < 0.001$). This finding supports the task specificity principle of motor learning. Skill training resulted in no changes in MEP magnitude. There was a trend ($p = 0.06$) towards increased submental muscles activity during functional swallowing tasks (i.e., non-effortful swallowing) in young subjects,. Males in skill training had decreased duration of UES opening in 10 mL water effortful swallowing task ($p = 0.02$), a trend towards increased UES pressure in non-effortful saliva swallowing task ($p = 0.07$), and reduced hyoid displacement following training ($p < 0.001$). Changes in pharyngeal pressures were detected for skill training with delayed visual feedback that resulted in decreased pressure at mid-pharynx in effortful and non-effortful tasks ($p < 0.05$). No difference in submental CSA changes was detected in either training group. Both groups improved motor performance measured by data collected during the session (target hit-rate and muscle activity).

The results of the pilot study that examined the effects of an extended dosage of training were difficult to interpret due to the small sample size. However, there were significant and marginally significant effects of skill training on mid-pharyngeal and UES pressure duration events.

Dysphagia is common in patients with Parkinson's disease, but no specific training programme exists for these patients, leading to the second question addressed through this research. Since movement planning is compromised due to dysfunction of the basal ganglia, providing external information for planning and executing swallowing was hypothesized to alleviate dysphagic symptoms. Ten subjects were recruited. Swallowing skill training with immediate feedback was administered for one hour every day, five days a week, for 2 weeks, similar to the training dosage and frequency in the healthy group. Biomechanical and structural changes were assessed. Swallowing skill training with immediate feedback led to an increase in submental activity in effortful swallowing tasks but not non-effortful tasks. In addition, it was found that individuals with dysphagia secondary to Parkinson's disease have decreased submental muscle reserve relative to healthy subjects.

Preliminary analysis of MEP data led to exploration of submental MEP measures between younger and older subjects. This 'discovery' research shed light on the third topic addressed in this thesis. There are contradicting results in the literature regarding age-related brain activity during swallowing. Since submental MEPs were included as an outcome measure in the main study, it was important to evaluate them at baseline in order to understand and interpret changes in this measure. Unlike other measures, such as pharyngeal pressure and hyoid displacement that have been documented in the literature to change with age, no similar study has been conducted to assess for differences in swallowing-related MEPs. Baseline data from the main study were analysed. Older subjects produced larger MEP magnitude in comparison to young in volitional saliva swallowing and volitional submental contraction. This finding raised some questions regarding the use of MEPs as an outcome measure, since it is not clear what constitutes a 'positive' change.

This study documented, for the first time, the application of skill training in swallowing in a healthy and dysphagic population. Positive effects of treatment were found in the dysphagic group; an indication of negative effects was identified in the healthy group. In addition, this is the first study to compare skill to strength training in swallowing. The only significant difference between the two was significantly greater submental activation in effortful swallowing tasks following strength training in comparison to skill training; although there were some significant interactions between age and training type and gender and training type. This project represents the first Phase I clinical-trial of an innovative approach for addressing swallowing impairments. Achieving the ultimate aim of finding the most appropriate training protocol for treating

individuals with a specific pathophysiological basis of dysphagia, requires the implementation of a long-term on-going research programme characterized by a staged process. This research programme sets an initial reference framework from which further projects can estimate the sample size required to answer specific questions, control for effects of age and gender and their interaction with training, increase precision in choosing assessment tools, and test new specific questions.

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Preface

This PhD thesis conforms to the referencing style recommended by the American Psychological Association Publication Manual (5th ed.) and spelling recommended by Oxford Dictionary.

The research for this PhD thesis was carried out between July 2010 and March 2012 while the candidate was enrolled in the Department of Communication Disorders, University of Canterbury. The research was based at the New Zealand Brain Research Institute, and was supervised by Dr Maggie-Lee Huckabee and Associate Professor Richard Jones. The candidate was supported by the University of Canterbury International Doctoral Scholarship.

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- Biomouth Symposium (Dunedin, June 2009)
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- Department of Communication Disorders Postgraduate Research Conference (Christchurch, November 2009)
- Biomouth Symposium (Christchurch, June 2010)
- The 8th Asia Pacific conference on speech, language and hearing (Christchurch, January 2011)
- The 7th Karlsbader Dysphagia Forum (Karlsbad, Germany, April 2011)
- Biomouth Symposium (Palmerstone North, November 2011)
- The 20th Annual Meeting of the Dysphagia Research Society (Toronto, Canada, March 2012) – awarded 2nd place New Investigator Award (oral presentation)
- University of Canterbury, Thesis in 3, university finals (Christchurch, August 2012)

Abbreviations

ANOVA	Analysis of variance
BA	Brodmann's area
BG	Basal ganglia
C1	Cervical spine nerve 1
C2	Cervical spine nerve 2
C3	Cervical spine nerve 3
C4	Cervical spine nerve 4
CI	Confidence intervals
CN	Cranial nerve
CN I	Cranial nerve 1
CN II	Cranial nerve 2
CN IX	Cranial nerve 9
CN V	Cranial nerve 5
CN VII	Cranial nerve 7
CN X	Cranial nerve 10
CN XII	Cranial nerve 12
CNS	Central nervous system
CPG	Central patterns generator
CSA	Cross sectional area
CSV	Comma-separated values
Cz	Cranial vertex
DSG	Dorsal swallowing group
EMG	Electromyography
EMST	Expiratory muscle strength training
ESLN	External branch of the superior laryngeal nerve
FMRI	Functional magnetic resonance imaging
GERD	Gastroesophageal reflux disease
GUI	Graphical user interface
ICC	Intra-class correlation coefficient
IOPI	Iowa oral performance instrument
ISLN	Internal branch of the superior laryngeal nerve
LES	lower esophageal sphincter
LMN	Lower motor neuron

LSVT	Lee Silverman voice treatment
LTD	Long-term depression
LTP	Long-term potentiation
M1	Motor strip, Brodmann's area 4
MEG	Magnetoencephalogram
MEP	Motor evoked potential
MG	Myasthenia gravis
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
NMES	Neuromuscular electrical stimulation
NTS	Nucleus tractus solitaries
PAS	Paired-associative stimulation
PD	Parkinson's disease
PET	Positron emission tomography
PP	Pharyngeal plexus
RLN	Recurrent laryngeal nerve
RM-ANOVA	Repeated measures analysis of variance
rTMS	Repetitive transcranial magnetic stimulation
S1	S1 Sensory strip, Brodmann's area 3, 1, 2
sEMG	Surface electromyography
SKL	Skill training
SKL-D	Skill training with delayed visual feedback
SKL-I	Skill training with immediate visual feedback
SLN	Superior laryngeal nerve
SMA	Supplementary motor area
STR	Strength training
SWAL-QOL	Swallowing quality of life
TBI	Traumatic brain injury
TES	Transcranial electrical stimulation
TMS	Transcranial magnetic stimulation
TOMASS	Test of mastication and swallowing of solids
TTL	Transistor-transistor logic
UC	University of Canterbury
UES	Upper esophageal sphincter
UMN	Upper motor neuron
VFSS	Videofluoroscopic swallowing study

VSG	Ventral swallowing group
WHO	World Health Organization

PART I: INTRODUCTION

CHAPTER 1 - INTRODUCTION

This thesis consists of four studies and is divided into five parts. *Part I* includes a literature review discussing healthy and disordered swallowing that supports all four studies. *Part II* of the thesis consists of the main study that documents the effects of swallowing skill training versus swallowing strength training in healthy subjects ($n = 40$), and includes a pilot study that describes the effects of increased dosage of training sessions in healthy subjects ($n = 10$) that took part in the main study. *Part III* of the thesis consists of a treatment pilot study that documents the effects of swallowing skill training in individuals with Parkinson's disease. *Part IV* consists of a baseline study that measured age effects on MEP characteristics. *Part V* includes a comprehensive discussion and conclusions.

Studies included in Parts II and III represent the first steps towards a more thorough approach to treatment outcome evaluation, and respond Logemann's suggestion (Logemann, 2005) for systematic assessments of the effects of swallowing intervention. She emphasized the need for documentation of training-related adaptations at different levels, such as neural, structural, and biomechanical, in healthy participants following training. Other investigators in swallowing rehabilitation (Gonzalez Rothi, Musson, Rosenbek, & Sapienza, 2008; Logemann, 2005; Ludlow et al., 2008; Robbins et al., 2008) have also recommended the translation of principles of neural plasticity into research in the area of communication disorders in general, and into dysphagia research specifically. A five-phase model for clinical research in communication disorders (Robey, 2004a) has been offered to assist in developing optimal interventions. In this regard, the main study includes objectives that represent the first phase of clinical-outcome research (Robey, 2004a; Rosenbek, 1995). As discussed in *Chapter 2 - Literature Review*, phase I research aims to develop the research hypotheses, assess safety, evaluate the treatment protocol, estimate the dose and measure the magnitude of the treatment effects. Since skill training has not been explored for its long-term effects, Phase I research was an appropriate starting point.

Part I – Introduction

Part I contains only *Chapter 2 - Literature Review*, which includes an in-depth discussion of swallowing biomechanics, neural control over swallowing, dysphagia complications, aetiology, and management. In addition, different measurement tools for assessing changes following behavioural swallowing training are discussed. The different phases included in clinical trials are reviewed as well.

Part II – Skill versus strength in swallowing training

The prevalent assumption in clinical practice is that dysphagia is a consequence of weak muscles (Clark, 2003), thus making strength training a common approach in rehabilitation. However, accuracy, speed of reaction, and timing of the multiple motor events are also important in swallowing. Dysphagia may also be due to impairment of the motor plan for swallowing (Daniels, 2000). An alternative approach of skill training has not been directly investigated in swallowing rehabilitation. The concept of skill training has emerged from other areas of research, mainly sport sciences, physiotherapy, and motor learning. Differences between strength and skill training have been investigated in the area of limb movement. Briefly, skill learning involves creation of new ‘specialized’ neural groups through synaptogenesis, enabling efficient and precise execution of skilled motor behaviour, without changing muscle strength. Hence, the cortex is the primary level at which changes occur. Strength learning in muscles of the limbs involves efficient efferent control during the execution of large forces due to adaptation in the activation of agonist, antagonist and stabilizing muscles, and leads to an increase in muscle strength. Neural adaptations following strength training affect the corticospinal downflow and the spinal motoneurons. This topic will be reviewed in *Chapter 3*, which provides a literature review specific to motor learning and includes a discussion on strength training and skill training effects.

Past research in swallowing rehabilitation has employed limited outcome measures, mainly focusing on biomechanical changes, and to a lesser degree – structural (muscular) changes, but has tended to disregard underlying neural effects. This has resulted in treatment paradigms that treat the end organ and are sometimes symptom based. Evaluation of treatment effects at the neural level can clarify the role of the central nervous system in rehabilitation of dysphagia and create possibilities for development of treatments that can be more suitable for dysphagia following neural damage.

The main study in this research programme evaluated a novel paradigm of skill training in swallowing compared to a more traditional approach of strength training based on effortful swallowing — a widely-used technique in clinical settings for treating individuals with dysphagia. Comparison between the two approaches consisted of differentiating the training effects at three levels: biomechanical, structural, and neural. Biomechanical assessments were comprised of measurements of pharyngeal pressures (peak pressure, duration and relative timing), hyoid displacement, and submental muscles activity. Structural assessment was comprised of measurement of the cross-sectional area of the submental muscles. Neurophysiological assessments were comprised of measurement of submental MEP magnitudes elicited by single-pulse TMS. Identifying differences between the two training approaches at each level could allow specific training protocols to be prescribed. In rehabilitation, training protocols should be based

on the unique pathophysiological basis of the impairment. Unfortunately, this is not common practice in swallowing rehabilitation.

The main hypothesis (see *Chapter 4 – Hypotheses*) was that skill training would more readily facilitate neural changes underlying functional swallowing than strength training, making it more suitable for patients with a neurological impairment. Subjects' performance during training was assessed in order to monitor fulfilment of the training goals. In order to assess compliance to the demanding schedule and to assess subjective perception of the training process, questionnaires were also completed by the participants.

As part of this research project, training software that utilizes submental muscle biofeedback to increase precision during swallowing was developed. Healthy adults were recruited, with age ranging from early 20's to late 80's (see *Chapter 5 – Assessments and Training Methods*). Dysphagia can occur at any age following a variety of medical conditions, including traumatic brain injury and stroke. In addition, since the most appropriate dysphagic populations for skill training have yet to be determined, overall effects were estimated using healthy subjects. This study included many outcome measures in an attempt to identify the main outcome measure for skill training.

An estimation of the effects of two different skill training protocols was carried out: skill training with immediate visual feedback and skill training with delayed visual feedback. *Chapter 5* includes a description of the two feedback protocols.

In order to document the effects of increased training dosage, a pilot study was conducted in parallel with the main study consisting of additional training sessions. Ten participants who took part in the two-week training protocol agreed to participate in the extended four-week training protocol that included the same assessments used in the two-week protocol.

Chapter 6 presents the results of the main study that compared skill to strength training. In addition, evaluation of the two skill training protocols and the increased-dosage pilot study are presented. *Chapter 7* consist of a discussion of these results.

Part III – Skill training in dysphagia

The effects of swallowing skill training were assessed in ten individuals with dysphagia secondary to Parkinson's disease as part of an associated pilot study. The literature supports the use of skill training approaches to rehabilitate some of the motor symptoms associated with Parkinson's disease. Similarly, dysphagia in patients with Parkinson's disease might be alleviated by training that emphasizes precise execution of swallowing. Skill training with immediate visual

feedback was used since the existing literature supports that patients with Parkinson's disease benefit from immediate feedback in voice and speech tasks (Coutinho, Diaféria, Oliveira, & Behlau, 2009). This study was designed and supervised by the project team (including the candidate) and the data were collected by a Masters student. A Master's thesis (Athukorala, 2012) has been written and some of the results are reported there. This current thesis reports outcome measures that were collected specifically for this project and were analysed by the candidate. The findings are presented and discussed in *Chapter 8*.

Part IV – Baseline differences in MEP characteristics

Although the larger scope of this thesis is the documentation of changes following swallowing training, an investigation of baseline differences between age groups and gender revealed unexpected age-related differences in submental MEP magnitudes that have not been reported in the literature. *Chapter 9* discusses these findings.

Part V – Final remarks and future research

Part V consists of *Chapter 10* that offers an over-arching discussion regarding the results of the three training studies (main study, extended-dosage pilot study, and skill training in individuals with dysphagia secondary to Parkinson's disease pilot study), and the results of the baseline study. This chapter includes concluding remarks and future directions for research.

CHAPTER 2 - LITERATURE REVIEW

2.1 Swallowing biomechanics

Swallowing is described as a complex sensorimotor behaviour that enables liquids and solids to pass from the mouth to the stomach (Donner, Bosma, & Robertson, 1985; Gleeson, 1999), serving a role in alimentary nutrition while protecting the airway (Jean, 2001). Ertekin (2011) distinguishes between two types of swallowing behaviours: swallowing can be voluntary – taking place when the individual consumes a bolus voluntarily, as part of eating – and it can occur spontaneously, due to accumulation of saliva or bolus residuals in the oral cavity, and serves a protection mechanisms (Ertekin, 2011).

Swallowing involves coordinated contraction and inhibition of 31 pairs of striated muscles (Dodds, Stewart, & Logemann, 1990) of the mouth, tongue, larynx, pharynx and oesophagus, occurring both concurrently and consecutively. The ‘leading complex’ of muscles that contract first during swallowing was investigated by Doty & Bosma (1956), and more recently by Thexton, Crompton, & German (2007). Both research groups examined the contraction pattern of the muscles involved in swallowing and identified the onset and peak of the electromyography (EMG) waveforms by placing intramuscular electrodes in those muscles in non-human mammals. Thexton et al. (2007) studied 16 of the muscles involved in swallowing in decerebrated pigs during purely reflexive pharyngeal swallowing, elicited by direct delivery of milk into the vallecula. Swallowing was monitored using videofluoroscopic swallowing study (VFSS), and ruled out oral phase involvement. They reported that 5 muscles: hyoglossus, stylohyoid, mylohyoid, middle pharyngeal constrictor and styloglossus composed the ‘leading complex’ and initiated their EMG activity before the onset of epiglottic tilting, which was chosen as the time-marker for the onset of the reflexive swallow. Doty & Bosma (1956) studied 22 muscles of the mouth, larynx and pharynx in monkey, dog and cat, which were either anesthetized intact or unanesthetized with an isolated encephalon. Three eliciting stimuli were used: electrical stimulation of the superior laryngeal nerve, tactile stimulation of the pharynx, and water injection to the vallecula. Detection of the swallowing event was based on visual examination of the EMG waveforms thus oral phase involvement was not controlled for. The leading complex consisted of mylohyoid, stylohyoid, and styloglossus (similarly to Thexton et al. (2007)), and superior constrictor, palate-pharyngeus, palatoglossus, geniohyoid, and posterior intrinsic muscles of the tongue.

The results of these two studies were not identical with regards to the composition of this 'leading complex', among which mylohyoid activity was reported to lead the other muscles by 30-40 ms by the earlier group (Doty & Bosma, 1956) but not by the later one (Thexton et al., 2007). Some differences were explained by Thexton et al. (2007) as existing variability in the activation of different motor units belonging to the same muscles. Since intramuscular electrodes were inserted into certain motor units, activation was inconsistently recorded, since the same motor unit do not fire constantly, with every swallow. This can account for earlier and later activation of the same muscles, and thus account for difference between the finding of the two research groups. Thexton et al. (2007) employed a non-parametric statistical method that utilized rank order statistics, using the median, which is less influenced by extreme data, rather than the mean. This might have reflected a more prevalent behaviour of motor-unit firing patterns, rather than sporadic activity. Following the activity of the leading complex, following a 30 ms lag, a second group of muscles became activated: medial pterygoid, palato-pharyngeus and omohyoid. Following that activity, anterior belly of digastric activity lagged by 40 ms, the thyrohyoid by 50 ms, the inferior constrictor by 70 ms, the geniohyoid by 120 ms, and the cricothyroid by 180 ms. Sternothyroid, strenohyoid and cricopharyngeus are activated last (lags of 250 ms, 270 ms, and 320 ms, respectively) (Thexton et al., 2007).

This pattern of activation reinforces the idea that swallowing is composed of interdependent components that overlap in time (Daniels & Huckabee, 2008; Martin-Harris, Michel, & Castell, 2005). Dividing the swallowing continuum into phases is somewhat artificial since there is temporal co-occurrence of events, and also one event affects the dynamics of other events (Martin-Harris et al., 2005). Nonetheless, categorizing this rapid and dynamic process into phases allows us to describe the swallowing process in an organized manner (Gleeson, 1999; Robbins, Hamilton, Lof, & Kempster, 1992). The traditional distribution of swallowing into three phases: oral phase followed by the pharyngeal phase, ending with the oesophageal phase, was based on descriptions of bolus flow (Doty & Bosma, 1956; Miller, 1982; Robbins et al., 1992). There are other descriptions that are also in use (Daniels & Huckabee, 2008; Dodds, Stewart, et al., 1990).

In the next section, the swallowing process will be described by dividing it into four phases: the pre oral phase, which was proposed by Leopold & Kagel (1997) and Daniels & Huckabee (2008), the oral phase which was described by Logemann (1998) and Perlman & Schulze-Delrieu (1996) in a manner that subdivides the events included into oral preparatory and oral transport phase, pharyngeal phase as was described by Perlman & Schulze-Delrieu (1996), and the oesophageal phase as was described first by Magendie (1825) (in Miller, 1982) and by Daniels & Huckabee (2008).

2.1.1 Phases of swallowing

2.1.1.1 Pre-oral phase of swallowing

Pre-oral features of swallowing occur prior to bolus entry to the oral cavity. The bolus characteristics of smell and appearance, and the attentiveness of the person consuming the bolus, influence this phase (Daniels & Huckabee, 2008). Other factors like hunger and motivation can also influence this phase (Kahrilas & Logemann, 1993). The chemo-receptors in the nose send information regarding smell, and the optic nerve sends information to the cortex regarding bolus size, texture, colour etc. The cortex processes this information and, in response, airway protection mechanism (Martin-Harris et al., 2005) and salivary secretion (Pedersen, Bardow, Jensen, & Nauntofte, 2002) may be initiated. Salivary gland secretion is initiated through activation of the conditioned salivary secretion reflex.

Briefly, salivary gland activation is controlled by a reflex arch that can be unconditioned and conditioned. Activation of the unconditioned reflex occurs following stimulation of chemo-receptors of the taste buds around the oral cavity and pharynx, and following stimulation of mechano-receptors in the oral cavity, specifically in the periodontal ligament (connective tissue that surrounds each tooth and attach it the alveolar bone). This information regarding taste is conveyed by CN VII (taste from the anterior 2/3 of the tongue) CN IX (taste and sensation from posterior 1/3 of the tongue) and CN VI (sensation from anterior 2/3 of the tongue and periodontal area). Smell (via CN I) can also contribute to initiation of salivation. Initiation of salivary flow can occur by a conditioned reflex. Seeing (CN II) and thinking about food can lead to increased salivary flow or, on the contrary, reduce it. For salivary flow to occur, the salivary nuclei send parasympathetic facilitatory signals via chorda tympani (CN VII) to the submandibular and sublingual glands and some minor glands. In addition, the salivary nuclei send parasympathetic signals via CN IX to the parotid glands. Sympathetic-autonomic signals from the salivary nuclei are sent to all three glands as well (Pedersen et al., 2002).

Vocal cord adduction and swallowing apnoea (cessation of breathing) can occur during this phase, before the onset of pharyngeal swallowing (Shaker, Dodds, Dantas, Hogan, & Arndorfer, 1990). This early onset of airway protection can be a result of a learnt response to drinking in a case of a liquid bolus (Martin-Harris et al., 2005) due to its brief transit time.

Leopold & Kagel (1997) termed this stage the “anticipatory stage” and described health conditions that may influence it, such as cognitive factors like decreased attention (e.g., in Alzheimer's disease), dystonia causing cervical hyperextension that distorts the anatomic position of structures (e.g., in progressive supranuclear palsy), and disorders of the basal ganglia (BG)

leading to excessive food intake ('stuffing') (e.g., in Parkinson's disease and Huntington's disease).

2.1.1.2 *Oral phase of swallowing*

The oral phase starts as the bolus enters the oral cavity. This phase involves the coordinated action of muscles of the lips, masticatory muscles, buccal muscles, tongue muscles, muscles of the soft palate, muscles connected to the hyoid bone, and submental muscles (Gleeson, 1999; Palmer, Rudin, Lara, & Crompton, 1992; Perlman & Schulze-Delrieu, 1996). In addition, saliva is secreted via the three salivary glands: submandibular, sublingual and parotid.

The oral stage can be subdivided into oral preparatory stage, which includes chewing and softening of the bolus until it is suitable for swallowing, forming it into a cohesive mass and collecting it at the middle of the tongue surface; and the oral propulsive or transit stage, which consist of the transference of the bolus from the oral cavity to the pharynx (Gleeson, 1999; Miller, 1982).

The oral phase length can change in response to bolus characteristics. For example, for a 10 mL liquid bolus, the duration of the oral phase is about 0.5 s (Dodds, Stewart, et al., 1990), but for a solid bolus the duration can be longer and exceed 20 s, with inter-subject and bolus type variations (Palmer, 1998).

2.1.1.2.1 *Oral preparatory stage*

At first orbicularis oris, which is the primary muscular component of the lips, receives an inhibitory neural command and relaxes, thus allowing labial opening and entry of the bolus to the mouth. If bolus size requires, the lips will be further spread by activation of facial muscles, such as levator labii superioris that raises the upper lip, risorius that retracts the corners of the mouth laterally and zygomaticus that lifts the corners of the mouth up and laterally. Jaw opening is achieved by the co-occurrence of 3 events: relaxation of jaw closing muscles (masseter, pterygoid, temporalis), hyoid bone stabilization by contraction of strap muscles of the neck, and jaw opening muscle contraction (mylohyoid, anterior belly of digastric, and geniohyoid) (Daniels & Huckabee, 2008).

After bolus entry, the lips seal the oral cavity. This seal forms the first pressure valve of the oropharyngeal pathway. The intrinsic and extrinsic muscles of the tongue contract and change the tongue contour to form a midline depression in which the bolus is contained prior to onset of its processing (Kahrilas, Lin, Logemann, Ergun, & Facchini, 1993).

Bolus type affects biomechanics during this phase. In the case of a small solid bolus or liquid bolus, the posterior portion of the oral tongue approximates the palate and creates a glossopalatal seal to contain the bolus within the oral cavity and prevent passage of the bolus to the pharynx prior to the initiation of the swallowing response. This glossopalatal seal is obtained by contraction of the palatoglossus muscles that elevates the tongue to approximate the hard palate, and contraction of stylohyoid, styloglossus and posterior belly of digastric muscles that pull the back of the tongue up and posteriorly. The processed bolus is formed into a cohesive mass that is contained in the space between the tongue's central groove and the palate which increases its depth with increasing bolus size (Kahrilas et al., 1993). For large boluses that cannot be swallowed at once, the glossopalatal junction serves as a divider between the portion of the bolus that will be swallowed and the portion that will stay in the oral cavity (Kahrilas et al., 1993). In these cases, there will not be complete glossopalatal seal according to the Process Model of Feeding offered by Palmer (Palmer et al., 1992), by which the bolus is chewed and softened, transferred to the oropharynx, including the vallecula, and aggregates there for 1 – 10 s while chewing continues (Hiieamae & Palmer, 1999).

Mastication involves the coordinated action of the intrinsic & extrinsic lingual muscles together with the masticatory muscles (jaw closing and jaw opening muscles) and buccinators to grind the bolus and mix it with saliva. The tongue moves the bolus to the occlusal surface of the teeth (the surface on the top of the molars), while the buccinators contract to prevent the accumulation of the bolus in the buccal cavity. Palmer, Hiieamae, & Liuf (1997) investigated jaw-tongue coordination during chewing. A temporal sequence of tongue movement and cyclical jaw motion was found in 70% of swallows documented. During jaw closing the tongue moves back and up. Immediately following, the teeth are at minimal distance and the tongue moves forward and up. During the early jaw opening stage, the tongue moves down and forward. Finally, at late jaw opening, the tongue moves down and back. Although this action is under volitional control, it is performed with little attention (Gleeson, 1999).

Saliva is secreted from the submandibular and sublingual glands via CN VII innervation and from the parotid gland via CN IX innervation. Taste buds around the oral cavity and mechanoreceptors around the teeth, palate, cheeks, and tongue are all stimulated during this phase. Afferent information from the tongue is conveyed via CN VII and CN IX for taste and via CN V and CN IX for touch. Mechanoreceptors around the teeth send afferent information via CN V, sensation from the soft palate is sent via CN VII, and sensation from the hard palate via CN V. The sensory information collected during the oral phase is carried by CNs V, VII, and IX are fed into nucleus tractus solitarius (NTS) of the medulla, and together with information collected during the pre-oral phase, participate in creation of the motor plan for swallowing.

2.1.1.2.2 *Oral propulsive or transit stage*

During this stage the glossopalatal seal is broken by depression of the back of the tongue to allow transference of the bolus into the oropharynx. In addition, the velum elevates to contact the posterior pharyngeal wall (see section 2.1.1.3 Pharyngeal phase of swallowing) and at the same time the lateral walls of the nasopharynx (superior constrictors) converge medially to facilitate contact and separate the nasopharynx from the oropharynx (Dodds, Stewart, et al., 1990). This separation, together with lip seal and contraction of the buccal muscle contract increases the pressure in the oral cavity.

The posterior tongue depresses and the anterior tongue elevates and presses against the hard palate to squeeze the bolus anteriorly to posteriorly in the oral cavity (Perlman & Schulze-Delrieu, 1996). The posterior oral tongue and the tongue base (pharyngeal tongue) (Figure 2.1) perform a centripetal motion followed by a centrifugal motion, however posterior oral tongue and tongue base motions are out-of-phase; thus this appears as a wavelike backwards motion on the tongue surface (Kahrilas et al., 1993). The tongue base moves inferiorly and anteriorly to expand the hypo-pharyngeal lumen to accommodate the bolus (Dodds, Stewart, et al., 1990).

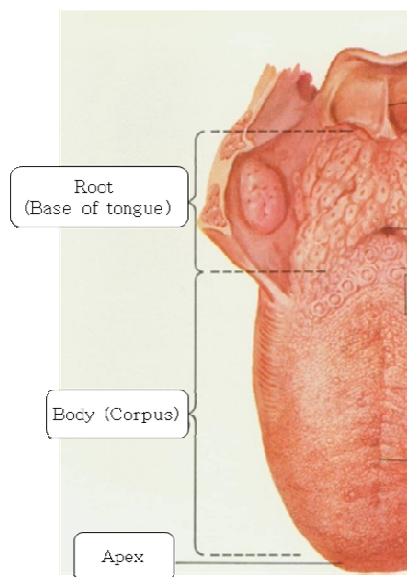


Figure 2.1 Dorsom (upper surface) of the tongue: Tongue's root (base of tongue, pharyngeal tongue), Body (Corpus, oral tongue), and Apex [from: <http://www.netterimages.com/image/8433.htm>].

During this phase *airway protection* mechanisms can be initiated or continued. Arytenoid approximation can occur (Ohmae, Logemann, Kaiser, Hanson, & Kahrilas, 1995) with or without true vocal fold approximation (Shaker et al., 1990). Swallowing apnoea can initiate during this phase, before the onset of pharyngeal swallow, but timing of onset is highly variable and can range from 16.7 ms to 7.33 s prior to hyoid excursion (Martin-Harris, Brodsky, Michel, Lee, & Walters, 2007). The oral phase ends at the onset of hyoid displacement, marking the onset of the pharyngeal response (Martin-Harris et al., 2007).

2.1.1.3 *Pharyngeal phase of swallowing*

The pharyngeal phase consists of several neuromuscular events that are highly synchronized and serve to propel the bolus from the oropharynx to the hypopharynx, and then to the entrance of the oesophagus (Daniels & Huckabee, 2008; Dodds, Stewart, et al., 1990). Three of the four swallowing pressure valves activate during this stage. Together with the first and most anterior valve - *lip seal* and buccal muscle tension as described earlier, the oropharyngeal space builds up pressure that drives the pharyngeal swallow and directs the bolus towards the oesophagus. The *velopharyngeal valve* separates the nasopharynx from the oropharynx to prevent air entrance from the open nasal cavity by elevation of the soft palate and the contraction of the pharyngeal wall. The *laryngeal valve* includes vocal cord adduction, epiglottis inversion and compression of the quadrangular membrane. In addition, the *cricopharyngeal valve* relaxes during swallowing and creates negative pressure as it opens to help propel the bolus into the oesophagus (Gleeson, 1999; Perlman & Schulze-Delrieu, 1996).

The marker of the onset of the pharyngeal swallow is onset of upward and forward hyoid movement (Martin-Harris et al., 2007). The offset of this phase is UES closure following transfer of the tail of the bolus through to the oesophagus (Robbins et al., 1992). During this phase, several events occur in synchrony: velopharyngeal closure, tongue base retraction, hyoid and laryngeal elevation, laryngeal valving, pharyngeal contraction, and UES opening (Daniels & Huckabee, 2008; Logemann, 1998). The pharyngeal phase has a relatively constant duration, indicating its reflexive and automotive control, lasting approximately 0.8 s to allow the bolus to transfer from the oropharynx to the oesophagus (Dodds, Stewart, et al., 1990; McConnel, Cerenko, Jackson, & Guffin, 1988)

Velopharyngeal closure

The onset of velopharyngeal closure is in close temporal proximity to the opening of the glossopalatal seal and bolus transference to the posterior oral tongue (Kahrilas et al., 1993). Velopharyngeal closure provides separation of the nasopharynx from the oropharynx. It consists

of movements in two directions: *elevation* of the soft palate towards the posterior pharyngeal wall through contraction of levator veli palatini and tensor veli palatini, together with *medial* movement of the posterior pharyngeal wall via contraction of palatopharyngeus and contraction of the superior pharyngeal constrictors that comprise the nasopharynx walls. The offset of velopharyngeal closure is in close temporal proximity to UES closure and the end of the pharyngeal swallow (Daniels & Huckabee, 2008; Kahrilas et al., 1993; Perlman & Schulze-Delrieu, 1996).

Base of tongue retraction towards the posterior pharyngeal wall

The tongue base is pulled posteriorly by activation of styloglossus, stylohyoid, posterior belly of digastrics and glossopharyngeus. This backward movement, together with convergence of the lateral and posterior pharyngeal wall, creates propulsive pressure on the descending bolus that drives the bolus through the oropharynx toward the hypopharynx (Dodds, Stewart, et al., 1990). This motion of the tongue is influenced by bolus size; as the bolus gets bigger there is an increase in propulsive tongue pressure but, for a smaller bolus, the pharyngeal constrictors increase their medial convergence motion to achieve both bolus propulsion and clearance (Kahrilas, 1993; Kahrilas et al., 1993).

Glottic closure

The vocal folds have a sphincteric function during swallowing (Shaker, Dua, et al., 2002). In order to prevent aspiration of the bolus into the trachea, the true vocal folds, the false vocal folds and arytenoids converge at midline by contraction of interarytenoids and lateral cricoarytenoid muscles. The posterior aspect of the cords is adducted by the interarytenoids muscles, while the anterior aspect is adducted by the lateral cricoarytenoids muscles. In addition, vocalis, cricothyroid and thyroarytenoid muscles increase the tension and contact of the folds (Shaker, Dua, et al., 2002). Together, these five intrinsic laryngeal muscles create closure of the glottis (Daniels & Huckabee, 2008; Matsuo & Palmer, 2009).

There is no uniform agreement regarding timing of vocal fold closure. Some studies found that the true vocal folds adduct before laryngeal elevation and hyoid movement (Shaker et al., 1990), and some found that that the true vocal folds close after the onset of laryngeal elevation (Ohmae et al., 1995). It seems that the timing of these events depends on bolus characteristic (Kahrilas, Logemann, Lin, & Ergun, 1992). The pressure created by vocal fold adduction is quite high, with a magnitude of 298 ± 23 mm Hg, which is similar to that produced during the valsalva manoeuvre (Shaker, Dua, et al., 2002).

Hyoid and laryngeal excursion

Initiation of hyoid excursion is one of the first markers of the onset of pharyngeal phase swallowing (Martin-Harris et al., 2007). Anterior hyolaryngeal excursion has an important role in airway protection and UES opening (Jacob, Kahrilas, Logemann, Shah, & Ha, 1989; Kahrilas, 1997; Steele et al., 2011).

The hyoid bone is pulled forward and upward by the anterior belly of digastric, geniohyoid and mylohyoid muscles, collectively referred to as floor-of-mouth or submental muscle groups (Jacob et al., 1989; Kahrilas, Logemann, Krugler, & Flanagan, 1991). The thyroid cartilage moves superiorly towards the hyoid by contraction of the thyrohyoid muscle, and since the thyroid is connected through muscles and ligaments to other laryngeal cartilages, these contractions result in elevation of the larynx and the anterior pharyngeal wall (Palmer, Tanaka, & Ensrud, 2000). This elevation of the hyoid and thyroid also contribute to pharyngeal shortening.

Different researchers have reported on different degrees of displacement. Overall, large variability can be attributed to differences in bolus densities and size, age groups and methodological factors between studies. Hyoid displacement can be calculated by measuring the distance between the hyoid position at rest and at maximum displacement (Dodds et al., 1988; Steele et al., 2011), or by measuring the displacement of other structures of the larynx like the arytenoids (Steele et al., 2011). *Anterior hyoid* displacement can range from 7.6 mm to 18 mm. *Superior hyoid* displacement can range from 5.8 mm to 25 mm (Molfenter & Steele, 2011). For both anterior and superior hyoid displacement, an increase in bolus size will result in an increase in hyolaryngeal movement. *Anterior laryngeal* excursion ranges from 3.4 mm to 8.2 mm and *superior laryngeal* excursion ranges from 21.1 mm to 33.9 mm (Molfenter & Steele, 2011). Again, there is increased displacement for larger bolus volumes (Molfenter & Steele, 2011).

The time lag between the arrival of the bolus head at the posterior angle of the mandible and onset of hyoid motion is important for airway protection. A long lag between these two events, with a later onset of hyolaryngeal elevation, is termed delayed pharyngeal swallow (Logemann, 1998; Robbins et al., 1992). Healthy participants, both young and old, can show a delay in pharyngeal swallow without any occurrence of aspiration. Thirty three - 43% of swallows were delayed, with a delayed onset of hyoid movement of approximately 220 ms (Martin-Harris et al., 2007). This delay might put an individual at risk of aspiration when it is accompanied by other impairments of swallowing physiology, but probably not when it is present in isolation (Martin-Harris et al., 2007).

Epiglottic inversion

As the hyoid and larynx move upwards and forwards, the larynx is displaced. Its position under the tongue base causes the epiglottis to tilt posteriorly; thus, the epiglottis tilts mechanically, rather than muscularly. Epiglottis inversion, together with arytenoid approximation towards the epiglottic base, forms a cover to the airway inlet. This closure has a role in increasing oropharyngeal pressures as well (Matsuo & Palmer, 2009).

Swallowing apnoea

Swallowing apnoea is an important event that serves to protect the airway from bolus entry during swallowing, together with other protective mechanisms like vocal cords closure. The timing of apnoea initiation is highly variable, and can range from 16.7 ms to 7.33 s before the onset of hyolaryngeal excursion with most healthy people commencing apnoea during the oral phase (Martin-Harris et al., 2005). The respiratory phase in which apnoea occurs can affect airway protection. Approximately 70% of healthy subjects exhale before and after swallowing, and approximately 20% inhale before and exhale after swallowing. Exhalation facilitates airway protection due to the para-median position of vocal folds during exhalation, as opposed to the abducted (open) position during inhalation. As the bolus starts passing through the pharynx, the inlet to the airways might still be exposed. Exhalation will create a positive pressure that will repel bolus entry to the larynx, whereas inhalation will create a negative pressure that might draw the bolus in. Following swallowing, exhalation can also serve to facilitate removal of any bolus remnants or saliva that might have penetrated the laryngeal vestibule, whereas inhalation may cause entry of bolus to the airway. Apnoea offset is highly correlated temporally to hyoid return to rest position (Martin-Harris et al., 2005).

Pharyngeal contraction

During swallowing, the pharynx both shortens and contracts and these two properties assist in bolus propulsion from the oropharynx to the hypopharynx, and in bolus clearance from the pharyngeal lumen to the oesophagus. Pharyngeal contraction is described as a stereotypic movement and is characterized by a constant propagation velocity, contraction force and pressure that create propagated horizontal contractions which are important for pharyngeal clearance (Kahrilas, 1993). The pharyngeal constrictors are also connected to the hyoid and thyroid cartilage, hence elevation of those structures results in pharyngeal shortening, to which stylopharyngeus contraction also contributes. The UES is elevated by approximately 2.2 cm (Kahrilas et al., 1992). This means that a total of 1.5 cm remains between the tongue base and the UES as a result of this shortening, requiring bolus transit through a relatively short distance

(Kahrilas, 1993). Pharyngeal shortening also reduces the volume of the pharyngeal lumen (Palmer, Tanaka, et al., 2000) and this reduction can contribute to the pharyngeal propulsive force and to creation of negative pressure.

Regarding temporal aspects, Palmer, Tanaka, & Siebens (1988) found that the pharynx first moved up, and then ventral and caudal motions of the pharyngeal walls follows. These motions form the contraction wave in the pharynx during swallowing, which is characterized by contractions of the superior constrictor followed by the middle constrictor and ends with the inferior constrictor contraction. The bolus is engulfed in this progressive wave of contractions and is propelled into the oesophagus (Palmer et al., 1988). During its descent, the bolus precedes the peristaltic wave; thus, pharyngeal contraction is creating pressure on the bolus tail (Donner et al., 1985).

UES relaxation

UES opening allows the bolus to transfer from the pharynx to the oesophagus. Opening depends on two components. First, the cricopharyngeus muscle (the main muscular component of the UES) which is tonically contracted at rest, relaxes. Second, the UES is mechanically opened due to submental muscle contraction and consequent anterior movement of the hyoid bone. This contraction results in hyolaryngeal excursion, which creates a traction force to pull the UES open. Sphincter relaxation precedes opening by approximately 10 ms (Kahrilas, Dodds, Dent, Logemann, & Shaker, 1988).

Onset of UES opening, duration and dimensions of opening, depend on bolus size. An increase in bolus size leads to longer duration of opening that is characterized by earlier onset and later offset of UES relaxation. Larger boluses also lead to increased diameter during opening (Kahrilas et al., 1988). UES opening is correlated in time with maximal laryngeal closure and maximal hyoid excursion (Martin-Harris et al., 2007). The UES becomes tonically active again once the bolus passes it (Jean, 2001; A. J. Miller, 1982).

2.1.1.4 *Oesophageal phase of swallowing*

This phase starts 600-900 ms following the initiation of the pharyngeal phase, when the bolus passes through the UES. It is composed of a sequential peristaltic wave of contractions, starting at the top part of the oesophagus and propagating towards the lower esophageal sphincter (LES), which lies at the entrance to the stomach. Transit time varies depending on the bolus type: liquids progress within 3 s (A. J. Miller, 1982), and solids can progress in 8-20 s (Dodds, Hogan, Reid, Stewart, & Arndorfer, 1973).

2.1.2 Summary

Swallowing can be divided into four phases. The pre-oral phase of swallowing consists of processing of cognitive input arising from presentation of the bolus, and the surrounding environment (Daniels & Huckabee, 2008), and is influenced from personal factors like motivation and awareness (Kahrilas & Logemann, 1993). The oral phase of swallowing can be subdivided into oral preparatory stage which includes bolus processing, and oral propulsive or transit stage that consist of bolus transfer into the pharynx (Logemann, 1998). This phase is mostly under voluntary control (Ertekin, 2011; A. J. Miller, 2008). The pharyngeal phase serves to propel the bolus from the oropharynx to the hypopharynx and then to the entrance of the oesophagus, and consists of several neuromuscular events, including velopharyngeal closure, tongue base retraction, hyoid and laryngeal elevation, laryngeal valving, pharyngeal contraction, and UES opening (Daniels & Huckabee, 2008; Logemann, 1998). This phase is under involuntary control (Ertekin, 2011; A. J. Miller, 2008), but can be volitionally modulated. The swallowing process ends with the oesophageal phase of swallowing which is under involuntary and autonomic neural control (Ertekin, 2011; A. J. Miller, 2008).

2.2 Neural control of swallowing

During swallowing, the central pattern generator (CPG) for swallowing in the brainstem becomes activated, together with other supranuclear structures. The CPG is responsible for programming the motor sequence of swallowing and consists of premotor neurons that communicate with the afferent and efferent levels. A network of control circuits exists between the different brain structures: CPG, cerebral cortex, cerebellum, putamen etc. These control circuits are responsible for planning, controlling, regulating and shaping swallowing (Ertekin, 2003; Miller, 2008; Mosier & Bereznaya, 2001).

In the past, the role of supranuclear brain structures was indirectly inferred from clinical observations of patients with dysphagia following cerebral lesions (Daniels et al., 1996). However, over the last 16 years there has been considerable progress in understanding the neural control of swallowing since application of direct assessment tools, like functional imaging examination, emerged in swallowing research.

In the following sections, the different brain structures, brainstem nuclei and cranial nerves (CN) related to swallowing are discussed. Assigning a specific function to each is somewhat artificial but it can allow us to better comprehend the basic role of the structure or nuclei, as we understand it today. Nevertheless, it is important to bear in mind that it is possible that identical insults to a

nerve or structure can result in different swallowing outcomes (Teismann et al., 2011), illustrating the complexity of neural control mechanisms over swallowing.

2.2.1 Upper motor neuron and lower motor neuron innervation of the muscle of swallowing

Upper motor neurons (UMN) have two pathways in which they can connect to the brainstem nuclei. The *direct pathway*, termed the *pyramidal tract*, is comprised of neurons that travel directly from the motor cortex to the brainstem nuclei. The *indirect pathway*, termed the *extrapyramidal tract*, is composed of multiple neurons that travel from the cortex to the brainstem nuclei, and synapse with neurons of other brain structures during their course of travel. UMNs synapse to nuclei of the CNs in two ways: by decussating (crossing over) at the pyramids (structures at the anterior portion of the medulla oblongata) and then synapsing on contralateral CN nuclei, or synapsing on ipsilateral CN nuclei (Duffy, 1995).

Most of the CNs related to swallowing receive bilateral input from the UMN, thus, the muscles involved in swallowing are bilaterally innervated. However, there are two exceptions. Muscles of the lower face, innervated by the facial nerve, receive only contralateral innervation from the UMN, while the upper face receives bilateral innervation (Figure 2.2). In addition, the genioglossus muscle, innervated by the hypoglossal nerve, receives only contralateral innervation from the UMN (Traurig, 2008). The rest of the tongue muscles, intrinsic and extrinsic, are bilaterally innervated. The degree of contralateral versus ipsilateral UMN control over muscles involved in swallowing has been investigated and the results indicate that contralateral innervation is greater than ipsilateral. For the masseter muscles (Butler, Miles, Thompson, & Nordstrom, 2001; Nordstrom et al., 1999; Ortu et al., 2008), anterior belly of digastrics (Gooden, Ridding, Miles, Nordstrom, & Thompson, 1999; Nordstrom et al., 1999), and mylohyoid muscles (Hamdy et al., 1996) (all innervated by the trigeminal CN), the contralateral projections were found to produce larger MEPs magnitude evoked by TMS than ipsilateral projections. The difference between the contralateral and ipsilateral MEPs, ranged from 30% to 85% (Nordstrom, 2007) with the masseter showing more asymmetry, thus more contralateral predominance, than anterior belly of digastrics (Butler et al., 2001; Gooden et al., 1999). Similarly, the tongue muscles innervated by the hypoglossus CN, have asymmetric cortical control, with greater contralateral cortical motor input than ipsilateral (Muellbacher, Artner, & Mamoli, 1999).

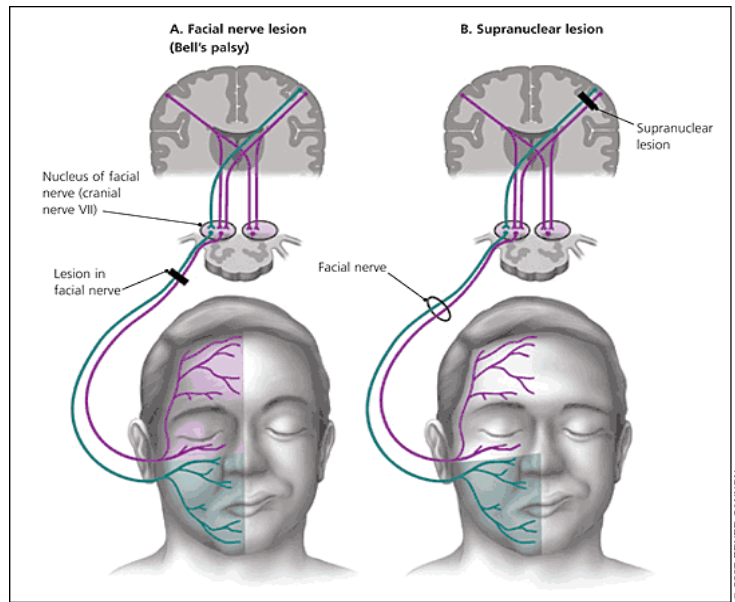


Figure 2.2 Facial innervation: Left: Damage to CN VII (lower motor neuron) results in upper and lower face paralysis or weakness. Right: upper motor neuron damage to face-M1 results in lower face paralysis
 [from http://erquiznpics.blogspot.co.nz/2011_02_01_archive.html].

Regarding hemispheric dominance, the right and left hemispheres produced similar amplitude MEPs following TMS stimulation for masseter muscle activation during a weak contraction of 10% of maximal voluntary contraction. This finding indicates no hemispheric dominance for masseter control (Ortu et al., 2008). The same was found for mylohyoid muscles (Hamdy et al., 1996). For anterior belly of digastrics muscles, hemispheric dominance was found to be task related: at rest and during voluntary contraction there was no difference between hemispheres, however during speech and jaw movement the left hemisphere had enhanced excitability when compared to the right (Sowman et al., 2009). Hemispheric dominance for pharyngeal control varied among subjects, with some showing more lateralization to the right and some to the left, with similar findings for oesophageal control (Hamdy et al., 1996).

From their nuclei, the lower motor neurons (LMN), which are effectively the CNs, send ipsilateral projections to the muscles they innervate. The junction between the LMN and the muscle is termed the *motor-end-plate*. The following section describes the CNs involved in swallowing.

2.2.2 Peripheral control

Swallowing requires the involvement of five CNs: V, VII, IX, X, XII. Some muscles in the pharynx are innervated by both IX and X CNs, and the term pharyngeal plexus is used to describe this common innervation. Ansa cervicallis also represents a combination of several neural

sources: CN XII together with nerves emerging from C1 to C4 in the spinal cord (Banneheka, 2008).

2.2.2.1 *Cranial nerve V*

The trigeminal nerve, the largest CN, is a mixed nerve that is composed mainly of sensory neurons but also has motor neurons (Borges & Casselman, 2010). It has three sensory nuclei that extend from the upper cervical spine to the pontomesencephalic junction: spinal trigeminal nucleus and tract, principal sensory nucleus and mesencephalic nucleus. The afferent neurons convey pain, temperature, tactile and kinaesthetic stimuli from the skin of the face and mucosa of the nose, mouth, palate and oropharynx (Prasad & Galetta, 2007; Walker, 1990). It has also one motor nucleus: the motor trigeminal nucleus located in the pons (Prasad & Galetta, 2007; Traurig, 2008). Its efferent neurons extend to the muscles of mastication and tensor veli palatini muscle.

This CN emerges from the lateral aspect of the pons and has 3 divisions (Borges & Casselman, 2010; Traurig, 2008), as its name implies. The *ophthalmic nerve* V1, is the first division. It conveys sensory information of pain, temperature and touch from the upper third of the face including the scalp, forehead, nose and cornea of the eye (Walker, 1990). V2, the *maxillary nerve*, is the second division. It carries afferent information from midface including the skin of the cheeks, lower eyelid, nares, nasal mucosa, upper lip, upper teeth and gums, soft and hard palate and nasopharynx (Prasad & Galetta, 2007; Walker, 1990). V3, the *mandibular nerve*, is the third and largest division of the three. It is composed of both sensory and motor neurons. *V3 sensory neurons* carry information from the lower face including the lower lip, lower teeth, chin, posterior cheek and mucosa of the lower part of the mouth and inner cheek. It also carries pain and touch sensations from the anterior two-thirds of the tongue (Prasad & Galetta, 2007; Walker, 1990). The sensory information is conveyed by CN V to the NTS indirectly (via the principal sensory trigeminal nuclei of the pons), and, thus, contributes to pharyngeal swallow elicitation together with sensory information from other CNs (A. J. Miller, 2008) and contributes to saliva secretion (Pedersen et al., 2002). Its motor root divides into branches: the *masticatory branch* that innervates the temporal, masseter, and medial and lateral pterygoid muscles, and the *mylohyoid branch* which innervates the mylohyoid and the anterior belly of the digastric muscle (Borges & Casselman, 2010). These muscles are used for opening (lateral pterygoid, anterior belly of digastric and mylohyoid) and closing (masseter, temporalis and medial pterygoid) the jaw, and moving the jaw laterally and medially (lateral and medial pterygoids), all of which are required for effective mastication (Prasad & Galetta, 2007). Hyoid excursion depends on the contraction of anterior belly of digastric and mylohyoid, together with geniohyoid muscle that is innervated by ansa cervicalis (Daniels & Huckabee, 2008). Another motor branch extends to tensor veli palatini,

which tenses the soft palate and assists the levator veli palatini muscle, innervated by pharyngeal plexus, to raise the soft palate during velopharyngeal closure.

Summary

CN V carries sensory information from the lips, teeth, gums, tongue, inner cheeks, palate and nasopharynx, which is important for bolus preparation and formulation into a cohesive mass, and plays a role in the afferent arm of salivary initiation reflex. Its efferent innervation has a primary role in mastication and thus, in bolus preparation during the oral phase. Together with other muscles innervated by different CNs, it contributes to soft palate elevation during oral transit, and hyoid excursion during the pharyngeal phase.

2.2.2.2 *Cranial nerve VII*

CN VII consists of three nuclei: facial motor nucleus located in the pons, the superior salivatory nucleus in the pons, and NTS in the medulla (Traurig, 2008). The facial nerve has a large root, consisting of 70% of the nerve fibres, that innervates muscles of the face, and a small root that consist of the other 30% of its axons, which carries parasympathetic innervation to the lacrimal, sublingual and submandibular salivary gland, and also carries afferent fibres that convey taste from the anterior two-thirds of the tongue (Brackmann & Fetterman, 2007; Traurig, 2008).

The motor nucleus is located in the reticular formation of the lower third of the pons, (Brackmann & Fetterman, 2007) in the lateral aspect of the pontomedullary junction (Traurig, 2008). It projects efferent fibres to the muscles of expression in the face and to two suprahyoid muscles: stylohyoid and posterior belly of digastric (Traurig, 2008). Thus it is involved in the oral and pharyngeal phases of swallowing. It innervates orbicularis oris, zigomatic, rizorios, quadratus labi superioris which open and spread the lips for bolus entry to the oral cavity, and during bolus preparation it innervates the same muscles to close and seal the oral cavity. This seal facilitates creation of pressure in the oral cavity and prevents leakage of the bolus between the lips during oral processing. The tongue base approximates the palate to maintain glossopalatal seal through the innervaion of a few CNs, with CN VII included. Activation of stylohyoid and posterior belly of digastric by CN VII contribute to this movement by elevating and retracting the tongue base. To allow bolus transfer to the oropharynx, stylohyoid and posterior belly of digastric contraction are inhibited, together with inhibition of other muscles that created the glossopalatal seal. Stylohyoid and posterior belly of digastric contraction also assist in transferring the bolus through the pharynx following bolus entry to the oropharynx by retracting the tongue base posteriorly, together with other muscles, which collectively generate superior pressure above the bolus (Daniels & Huckabee, 2008). CN VII also innervates the buccinators that contract during the oral

phase, to maintain the bolus on the teeth surface during chewing, and prevent the bolus accumulation in the buccal sulcus. CN VII innervates the platysma muscle that depresses the lower lip, and depresses and pulls the corners of the mouth laterally during the oral phase in case of a big bolus. The platysma depresses the mandible (together with anterior belly of digastric, mylohyoid, and geniohyoid) during the oral phase to allow mouth opening. The motor nucleus of CN VII has different corticonuclear innervation when compared to other CNs. The upper half of the face receives bilateral innervation from the cortex, but the lower half receives contralateral innervation only (Traurig, 2008).

Afferent fibres conveying taste from the anterior two-thirds of the tongue and from the soft palate are fed into the NTS of the medulla via the chorda tympani (McManus, Dawes, & Stringer, 2011). Taste from the tongue, together with taste and other sensations from the oral and pharyngeal cavity are important for eliciting the pharyngeal swallow (Daniels & Huckabee, 2008; A. J. Miller, 2008) and also in eliciting salivary flow (Pedersen et al., 2002). Two out of the three salivary glands: the sublingual and submandibular glands are innervated by CN VII. The two receive parasympathetic innervation via the chorda tympani branch of CN VII leaving the superior salivatory nucleus in the pons (McManus et al., 2011). The submandibular gland accounts for 70% of salivary secretion (Cunning, Lipke, & Wax, 1998). Salivary secretion has an important role in mastication and bolus formation (Pedersen et al., 2002) thus, during the oral phase of swallowing.

Summary

CN VII has an important role during the oral phase of swallowing and a secondary role during the pharyngeal phase. Its primary role is in innervating muscles that seal and open the mouth, and in creating tension in the cheeks to assist with effective bolus preparation. It also participates in creating glossopalatal seal to prevent bolus spillage into the pharynx during bolus preparation. During the pharyngeal phase, CN VII innervates muscles that participate in transferring the bolus through the pharynx by creating pressure above the descending bolus. The afferent fibers of the chorda tympani branch convey taste from the anterior two-thirds of the tongue, and provide parasympathetic innervation to two salivary glands, thus contributing to bolus preparation during the oral phase.

2.2.2.3 *Cranial nerve IX*

The glossopharyngeal nerve originates as several bundles from the lateral aspect of the medulla, just inferior to the pontomedullary border (Traurig, 2008). The three glossopharyngeal nuclei are located in the rostral medulla. The *inferior salivatory nuclei* provide visceral efferent fibres to the

parotid glands for saliva secretion. The *nucleus ambiguus* on either side send ipsilateral efferent innervation to the stylopharyngeus muscle that contributes to laryngeal elevation and pharyngeal expansion and shortening (Traurig, 2008). The bilateral NTS receive afferent fibres that convey pain, temperature and tactile information from the mucosa of the middle ear cavity, oropharynx, eustachian tube and tonsils, and also carries taste, pain, temperature and touch from the posterior third portion of the tongue (Hermanowicz, 2007). CN IX provides the afferent limb of the gag reflex, which consists of elevation and constriction of the pharynx and retraction of the tongue in response to tactile stimulation of the pharyngeal wall, back of the tongue, tonsils or faucial pillars (Hermanowicz, 2007). The pharyngeal plexus conveys the efferent limb of this reflex.

Summary

CN IX has an important role in the pharyngeal phase of swallowing, by carrying afferent and efferent information to the pharynx, mostly together with CN X (see: Pharyngeal plexus - 2.2.2.5). It innervates the stylopharyngeus muscles and the parotid glands independently, and carries sensory information from the oropharynx and posterior third of the tongue. Together with the pharyngeal plexus, it innervates the gag reflex response.

2.2.2.4 *Cranial nerve X*

The vagus nuclei are located in mid-medulla and include the shared *nucleus ambiguus* (with CN IX and XI) and the shared NTS (with CN VII and IX) that pertain to swallowing, and the *dorsal motor nucleus* of the vagus that is not related to swallowing (Traurig, 2008). The vagus nerve has a role in swallowing, voicing, and respiration, as well as other roles associated with the cardiovascular and gastrointestinal systems.

Each vagus nerve is divided to a superior laryngeal nerve (SLN) and a recurrent laryngeal nerve (RLN). The internal branch of the superior laryngeal nerve (ISLN) carries sensory information from above the level of the vocal folds (including the base of tongue, aryepiglottic fold and epiglottis). Electrical stimulation of the ISLN can elicit reflexive swallowing (Doty, Richmond, & Storey, 1967). The external branch of the superior laryngeal nerve (ESLN) innervates the cricothyroid, which elongates the vocal folds and increases the tension within the fold. The RLN innervates the intrinsic muscles of the larynx, except for cricothyroid, and carries sensory information from and below the glottis including the oesophagus. The interarytenoid and cricoarytenoid muscles, two of the intrinsic laryngeal muscles, contract to adduct the vocal cords and protect the trachea during swallowing (Chitkara, 2006). The cricopharyngeus (CP), which is the main muscle that composes the UES, is tonically contracted by excitatory efferent signal. There are conflicting reports regarding its exact innervation pattern (Ertekin & Aydogdu, 2002).

Sasaki et al. (1999) found that the RLN innervates the anterior motor unit of the CP and the pharyngeal plexus innervates the posterior motor units (Sasaki et al., 1999), whereas others (Prades et al., 2009) found RLN innervation to the posterior part of the CP, and ESLN innervation to the anterior part of the CP. The UES relaxes during swallowing as inhibition of the neural signal occurs to allow the bolus to pass from the hypoharynx to the oesophagus (Kahrilas et al., 1988; A. J. Miller, 1982).

The vagus mediates the afferent and efferent arms of the reflexive cough response. Cough is an airway defence response that generates high velocity airflow to remove mucus or foreign bodies from the airway. Sensory information from receptors of the larynx and lower airway is conveyed by vagal afferent fibres that are fed into the NTS. The efferent arm of the cough response consists of sequential activation of laryngeal and respiratory muscles, hence, involves several additional nerves and nuclei. The respiratory muscles are activated via interconnection between the respiratory dorsal and ventral groups of the medulla and the phrenic, intercostals and lumbar nerves. In addition, the motor command is conveyed via the vagus that innervates the laryngeal intrinsic muscles. Lastly, sympathetic and parasympathetic nerves supply the airway smooth muscle and glands (Fontana & Lavorini, 2006).

Summary

The vagus has an important role in swallowing and in airway protection mechanisms through vocal fold adduction and cough reflex response. It carries sensation from the larynx and oesophagus and innervates the intrinsic laryngeal muscles and the cricopharyngeus which is the main muscle of the UES (Perlman & Schulze-Delrieu, 1996).

2.2.2.5 *Pharyngeal plexus*

The pharyngeal plexus (PP) is composed of the glossopharyngeal and vagus nerves. As mentioned before, the nuclei of these CNs lie in the medulla. The PP nerves are formed by rootlets that emerge from the lateral medulla and travel in proximity (Traurig, 2008).

The PP innervates the palatoglossus muscle that is the main muscle responsible for approximation of the posterior oral tongue to the palate during the oral phase. Levator veli palatini is also innervated by PP. This muscle, together with tensor veli palatini (CN V), contracts and closes the velopharyngeal port and separates the nasopharynx from the rest of the pharynx, hence resulting in increased pressure within the pharyngeal space and on the bolus. PP innervates the glossopharyngeus muscle (a component of the superior pharyngeal constrictor) that contracts and retracts the tongue base to the posterior pharyngeal wall, together with other muscles, to increase

the pressure on the descending bolus, as it moves from the oropharynx to the hypopharynx (Perlman & Schulze-Delrieu, 1996). The pharyngeal constrictors (superior, middle and inferior) are also innervated by PP. They clear the bolus from the pharynx by creating propagating horizontal contractions (Kahrilas, 1993). As mentioned previously, some suggest that the PP innervates the posterior motor unit of the CP muscle (Sasaki et al., 1999). Salpingopharyngeus and palatopharyngeus are both innervated by PP and contribute to pharyngeal shortening through elevation of the pharynx resulting in a shorter distance between the UES and the bolus (Donner et al., 1985; Kahrilas, 1993). PP carries sensory information from the oropharynx and hypopharynx to the NTS, thus allowing sensation of residuals in the pharynx.

Summary

The PP conveys afferent and efferent innervation to most of the pharyngeal muscles thus has a crucial role during the pharyngeal phase of swallowing. It sends efferent innervation to levator veli palatini, glossopharyngeus, the pharyngeal constrictors (and possibly to the CP muscle), to salpingopharyngeus, and to palatopharyngeus. In addition it plays a role during the oral phase through the activation of palatoglossus.

2.2.2.6 *Cranial nerve XII*

The hypoglossal nucleus extends throughout the dorsal aspect of the medulla, and its nerve arises from a line of rootlets located in the medulla, between the pyramids and the inferior olivary nucleus (Traurig, 2008). The nerve provides motor innervation to the intrinsic muscles of the tongue that contours the tongue: the superior and inferior longitudinal muscles which shorten and curls the tip superiorly and inferiorly, respectively; the transverse muscle which shortens the tongue; and the vertical muscle which flattens it. CN XII is also efferent to the extrinsic muscles of the tongue that change the tongue's position in the oral cavity: genioglossus, styloglossus, and hypoglossus. Genioglossus is a fan-like muscle that is composed of the horizontal genioglossus that pulls the tongue base forward, and the oblique genioglossus that pulls the tongue body downward. Styloglossus retracts and elevates the tongue. Hypoglossus retracts and depresses the tongue (Daniels & Huckabee, 2008; Mu & Sanders, 2010).

The hypoglossal nerve has two branches. The lateral branch supplies the superior longitudinal, inferior longitudinal, styloglossus, and hyoglossus muscles. The medial branch supplies the genioglossus, transverse, vertical and inferior longitudinal muscles (Mu & Sanders, 2010) (Figure 2.3). As mentioned before, the nerve's nuclei receive bilateral corticobulbar innervation, except for the genioglossus muscle, which receives predominantly contralateral innervation (Traurig, 2008).

Summary

The hypoglossal nerve has an important role during the oral phase. It activates the tongue muscles that create a channel-like curve at the midline of the tongue to contain the bolus as it enters the mouth, transfer the bolus to the teeth for chewing, and transfer the bolus from its anterior position to a posterior position in the oral cavity by applying pressure on it when it is ready to be swallowed. The complex movements of the tongue involve two muscle groups: intrinsic muscles that change the tongue's contour, and extrinsic muscles that change its position.

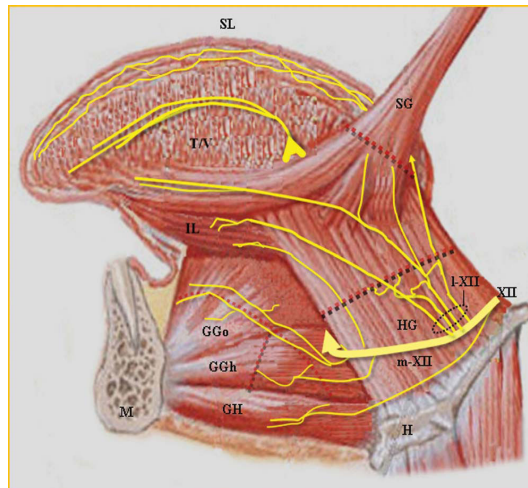


Figure 2.3 Illustration of the tongue muscles and the motor innervation by cranial nerve XII, in a lateral view of a sagittal section. XII- hypoglossus cranial nerve; l-XII- lateral branch of CN XII; SL- superior longitudinal; SG- styloglossus; HG- hypoglossus; IL- inferior longitudinal; m-XII- medial branch of CN XII; GG- genioglossus, GGo - GG oblique, GGh - GG horizontal; T/V- transverse; M- mandible; H- hyoid [from Mu & Sanders (2010)].

2.2.2.7 Ansa cervicalis

Ansa cervicalis is composed of CN XII and spinal nerves that arise from C1 to C4 of the cervical spine. It has two roots: the *superior root* that is composed of CN XII and C1 and C2, and the *inferior root* that varies in its segmental composition among healthy adults. Different studies documented the following variation in composition of the inferior root: C1 & C3, C2-C3, C2-C4, C3 or C2 (Banneheka, 2008; Loukas et al., 2007). The ansa cervicalis innervates the infrahyoid muscles and the geniohyoid.

The superior belly of omohyoid and the superior part of sternohyoid are usually innervated by C1 and C2. Inferior belly of omohyoid has variable innervation among people, with different composition of C1, C2 and C3. Sternothyroid and the inferior part of sternohyoid are usually

innervated by all cervical spine segments (C1-C4) (Banneheka, 2008). Thyrohyoid is innervated by C1 & C2 (Banneheka, 2008) or a combination of XII, C1 & C2 (Kikuchi, 1970) and geniohyoid is innervated by XII, C1 & C2 (Banneheka, 2008; Kikuchi, 1970).

The infrahyoid muscles, also called strap muscles, contract to fix the hyoid bone in place. Hyoid fixation also depends on contraction of the jaw opener muscles (anterior belly of digastric, mylohyoid and geniohyoid), and relaxation of jaw closer muscles (temporalis, masseter and pterygoid). In addition, contraction of thyrohyoid contributes to supraglottic shortening, resulting in protection of the airways during the pharyngeal phase (Palmer, Drennan, & Baba, 2000). Geniohyoid muscle contraction contributes to hyoid excursion and epiglottic deflection together with anterior belly of digastric and mylohyoid which are innervated by CN V.

Summary

Ansa cervicalis innervates the geniohyoid muscles, which take part in hyoid excursion, and thyrohyoid muscles that contribute to supraglottic shortening. In addition, it also innervates the infrahyoid muscles (omohyoid, sternohyoid, and sternothyroid) that depress the hyoid bone.

2.2.3 Brainstem control of swallowing

The pons and medulla oblongata, two brainstem structures, contain the nuclei of the CNs that innervate the swallowing muscles. The medulla also houses the CPG for swallowing that controls and shapes the reflexive swallow. The role of the brainstem nuclei and CPG have been studied since the beginning of the 20th century (Miller, 1920).

Evidence for brainstem control of swallowing emerged mainly from invasive animal studies (Doty et al., 1967; Ertekin & Aydogdu, 2003; Jean, 1984, 2001; Jean, Amri, & Calas, 1983; Kessler & Jean, 1985), or from clinical observation of dysphagic patients (Martino, Terrault, Ezerzer, Mikulis, & Diamant, 2001). Functional magnetic resonance imaging (fMRI) (Komisaruk et al., 2002) and magnetic resonance imaging (MRI) studies (Chen & Huang, 2008; Warabi et al., 2008) also offer insight regarding the brainstem role in swallowing.

Doty (1968) stated that swallowing-related brainstem neural structures have three components or levels: (1) afferent input from the swallowing tract carried by CN 5, 7, 9 and 10, (2) efferent output to the swallowing muscles carried by CNs 5, 7, 9, 10 and 12, and (3) an organizing level that consists of an interneuronal network of ‘premotor’ neurons that communicates with the afferent and efferent levels. This network of premotor neurons functions as a CPG that is responsible for programming the motor sequence of swallowing (Broussard & Altschuler, 2000; Doty, 1968; Jean, 1984, 2001). Jean and others (Jean, 1984; Jean et al., 1983; Jean & Car, 1979;

Kessler & Jean, 1985) localized the CPG in a cat, sheep and rat using microelectrodes. They stimulated certain regions of the medulla oblongata, and found that neural stimulation of certain areas resulted in contraction of muscles related to swallowing. Jean summed up the findings from his and others experiments as follows. The CPG is composed of the dorsal swallowing group (DSG), corresponding to the NTS and adjacent reticular formation, and the ventral swallowing group (VSG), corresponding to the ventrolateral reticular formation above the nucleus ambiguus (Jean, 1984). Two hemi-CPGs exist, one on each side of the medulla, with connections between the two VSG (Jean, 2001).

The DSG contains neurons that are involved in initiating, shaping, and timing the sequential swallowing pattern. DSG activity was found to be independent of muscular contraction, and sensory feedback, supporting its role in organizing the swallowing sequence (Jean, 1984). In addition, recordings of neural activity from this area exhibited firing in a sequence similar to the observed muscle activity (Jean, 1984). The DSG has been shown to be activated before the onset swallowing, indicating its involvement in swallowing motor planning, organization and initiation. When neurons within the NTS were destroyed, swallowing was not elicited following stimulation of the frontal cortex (Jean & Car, 1979) and the superior laryngeal nerve (Kessler & Jean, 1985), both of which, in the presence of an intact NTS, would result in a swallowing response.

Connections between the DSG and VSG have been documented. Following SLN or frontal cortex stimulation, neural activity was measured first at the DSG and then at the VSG. In addition, electrophysiological recordings documented similar firing patterns between the DSG and VSG (Jean, 1984; Jean & Car, 1979; Kessler & Jean, 1985).

Experiments involving injection of tracing substance found that the VSG sends axons to the trigeminal motor nucleus (Jean et al., 1983). This finding supports the notion that the VSG consist of switching neurons that distribute the command for excitation/inhibition of various motoneurons pools motoneurons involved in swallowing (CN 5, 7, 9, 10 and 12) (Jean, 2001; Jean et al., 1983). Hence, it is assumed that the VSG is involved in execution and is probably activated by the DSG, where the swallowing plan is being formed (Jean, 1984).

To summarize, the medulla and the pons house the CPG and CN nuclei for swallowing. Sensory information is carried by afferent nerves that feed into the CN nuclei. Information from these sensory nuclei feeds into the DSG that plans and shapes the swallowing event. Interneurons transfer this information to the VSG that organize and execute the motor plan, by distributing the motor command to the appropriate motoneurons (Figure 2.4).

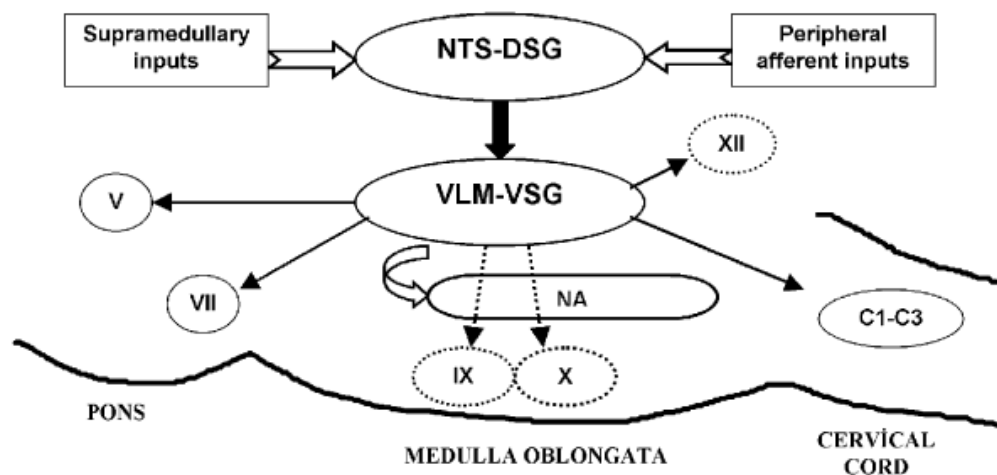


Figure 2.4 Schematic representation of the swallowing CPG. Sensory information from peripheral CNs (CN V, VII, IX, X) and from supramedullary areas feed into the DSG (that includes the NTS) located at the dorsal aspect of the medulla. The DSG activates the VSG that is located in the ventrolateral medulla (VLM). The VSG drives the motoneurons of CNs IX & X via nucleus ambiguus and CNs V, VII, XII and C1-C3* of the cervical spine. [from Ertekin & Aydogdu, 2003] *some suggest C1-C4, see text regarding ansa cervicallis composition.

2.2.4 Supranuclear control of swallowing

Evidence concerning supranuclear areas involved in swallowing has emerged from studies using neuroimaging techniques including fMRI (Humbert et al., 2009; Kern, Jaradeh, Arndorfer, & Shaker, 2001; Martin, Goodyear, Gati, & Menon, 2001; Suzuki et al., 2003; Toogood et al., 2005; Zald & Pardo, 1999), and Positron Emission Tomography (PET) (Hamdy, Rothwell, et al., 1999). In addition, neurophysiological techniques have been utilized to study neural control of swallowing, including TMS (Abdul Wahab, Jones, & Huckabee, 2010; Al-Toubi, Abu-Hijleh, Huckabee, Macrae, & Doeltgen, 2011; Doeltgen, Dalrymple-Alford, Ridding, & Huckabee, 2010; Hamdy, Aziz, Rothwell, Hobson, et al., 1997; Power et al., 2004), magnetoencephalography (MEG) (Teismann, Dziewas, Steinstraeter, & Pantev, 2009), and electroencephalography (EEG) (Huckabee, Deecke, Cannito, Gould, & Mayr, 2003).

Neural activity associated with swallowing has been recorded in several cortical loci (Miller, 2008) including the precentral gyrus, postcentral gyrus, supplementary motor area (SMA), premotor area, cingulate cortex, insula, the superior temporal gyrus, middle and inferior frontal gyri, and frontal operculum (Martin et al., 2001; Mosier & Bereznaya, 2001). Different studies identified activation in different locations due to differences in study design, tasks given, age of the participants and technical features of the scan, thus not all studies identified the same areas.

The following sites of activation have been reported in several studies:

The *precentral gyrus* (*BA4* also called *M1*) is suggested to take part in initiating the swallowing sequence, and in modulating and priming the pharyngo-oesophageal component of swallowing (Ertekin & Aydogdu, 2003; Fraser et al., 2002; Hamdy, Mikulis, et al., 1999; Kern, Jaradeh, et al., 2001; Martin et al., 2004, 2001; Mosier & Bereznaya, 2001; Mosier, Liu, Maldjian, Shah, & Modi, 1999; Suzuki et al., 2003). Intracortical electrical stimulation in the awake monkey revealed interesting findings regarding M1 role in swallowing. Superficial (less than 5 mm deep) stimulation of face-S1, face-M1, or the cortical masticatory area (CMA) elicited masticatory sequence with or without swallowing. Swallowing in isolation (without associated jaw or orofacial movements) was evoked predominantly from areas within the deep cortical region. The area location and depth (5-8 mm deep) correspond to the white matter and frontal operculum that lie under the rostral (front) aspect of the posterior CMA. This finding suggested that M1 contains sites that function as the primary cortical area for swallowing. In addition, swallowing in isolation was evoked from the face-M1 and the posterior cortical masticatory area (< 5 mm depth). Stimulation of the same areas also elicited swallowing accompanied with other orofacial movements. This suggests that the face-M1 might play a role in driving motoneurons innervation to muscles involved in swallowing although this hypothesis has not been confirmed. Swallowing occurrence was confirmed by examination of EMG waveforms recorded from genioglossus muscles and thyrohyoid and cricothyroid, by comparison of the EMG waveforms found in the experiment to control waveforms recorded in intact monkeys while swallowing, and by direct observation during the study (Martin et al., 1999). Since the experiment was conducted on intact animals with functioning brainstem, it is difficult to isolate the role of the cortex in swallowing initiation as suggested by the authors. It is known that cortical input feeds into the DSG of the medulla, but the provided sensory information fulfils only one 'arm' in swallowing initiation.

Swallowing-related areas in M1 were assessed with TMS to measure excitability as reflected by MEP amplitude and latency, and to measure cortical representation maps of swallowing related area. Swallowing-related MEPs were recorded from the submental muscle group (Abdul Wahab et al., 2010; Al-Toubi et al., 2011; Doeltgen et al., 2010) pharynx (Fraser et al., 2002, 2003; Hamdy, Rothwell, Aziz, Singh, & Thompson, 1998) and oesophagus (Aziz et al., 1994; Fraser et al., 2003; Hamdy, Rothwell, et al., 1998). Studies conducted on healthy participants indicated that the mylohyoid muscle was represented bilaterally and symmetrically, with greater MEP amplitude from the contralateral muscle compared to the ipsilateral muscle to the hemisphere stimulated (Hamdy et al., 1996). In most subjects, pharyngeal MEPs and oesophageal MEPs were evoked from both hemispheres, however the number of cortical sites evoking the MEP response from the pharyngeal and oesophageal muscles was asymmetrically represented between the two

hemispheres with some subjects showing more sites on the right and some having more sites on the left, regardless of handedness. This finding led the authors to believe that a swallowing-dominant hemisphere exists (Hamdy et al., 1996; Hamdy, Aziz, Rothwell, Crone, et al., 1997).

Hemispheric dominance for anterior belly of digastric muscle was found to depend on the task: during rest and contraction similar MEP responses were recorded following stimulation of either the right or left hemispheres, but during speech and jaw movement, TMS over the left hemisphere resulted in greater MEP magnitude in comparison the right side (Sowman et al., 2009). This might be related to left hemispheric dominance in speech. This study also suggests that since digastric participates in several motor behaviours, the motor control changes according to the task, thus it is possible that its activation during swallowing will have different control mechanism. MEPs recorded from the masseter during minimal contraction of 10% of the maximal voluntary contraction capacity were similar from right and left hemispheres (Ortu et al., 2008) and, thus, for low-level contraction there is bilateral and equal motor control.

The bilateral control (whether it is symmetrical or asymmetrical) over the muscles participating in swallowing might be related to reports regarding rapid recovery rate following cortical stroke in comparison to recovery following brainstem stroke. Although Hamdy et al. suggested that injury to the swallowing dominant hemisphere can be detrimental, and be characterized by reduced recovery, the evidence to support this hypothesis was based on 20 subjects (Hamdy, Aziz, et al., 1998). Larger scale studies will help to elucidate the role of M1 in swallowing, and would be useful for creating adequate rehabilitation programmes for dysphagia.

The *postcentral gyrus* (BA 3, 1, 2 also called *S1*) and the parietal cortex are suggested to be involved in regulating and modulating swallowing by processing swallowing-related afferent information and conveying it to the precentral gyrus (Ertekin & Aydogdu, 2003; Fraser et al., 2002; Hamdy, Mikulis, et al., 1999; Kern, Jaradeh, et al., 2001; Martin et al., 2004, 2001; Mosier & Bereznaya, 2001; Mosier, Liu, et al., 1999; Suzuki et al., 2003). Intracortical electrical stimulation of the primary sensory face area was also documented to evoke orofacial and jaw movements with or without swallowing. However swallowing in isolation was not elicited following face-S1 stimulation (Martin et al., 1999).

The *insula* is frequently reported to be activated during swallowing (Ertekin & Aydogdu, 2003; Hamdy, Rothwell, et al., 1999; Kern et al., 1998; Kern, Jaradeh, et al., 2001; Mosier, Patel, et al., 1999; Mosier & Bereznaya, 2001). One possible reason is due to taste representation in the insula, which is supported by its activation during both voluntary and automatic swallowing (Martin et al., 2001). The insula has been suggested to have a role in mediating the sensory and motor aspects of the gastrointestinal tract, including the oropharynx and oesophagus (Binkofski et al.,

1998; Kern et al., 1998). Lesions in the anterior insula are associated with the presence of dysphagia with delayed pharyngeal swallowing (Daniels & Foundas, 1997). It has thus been suggested that the anterior insula is involved in the initiation of swallowing (Watanabe, Abe, Ishikawa, Yamada, & Yamane, 2004), supported by the finding of insular activation prior to the onset of swallowing. The earlier insular activation found by Watanabe, Abe, Ishikawa, Yamada, & Yamane (2004), was not found by Hamdy et al., 1999. In addition, earlier activation does not necessarily support the role of the insula in swallowing initiation. The insula has connections with the primary and supplementary motor areas (Martin & Sessle, 1993) and with the NTS (Beckstead, Morse, & Norgren, 1980). This might support the role of supramedullary regions in providing afferent information to the DSG of the medulla, in addition to sensory information from CNs involved in swallowing (Jean, 2001). The DSG creates the motor plan for swallowing relaying on the sensory information. Daniels & Foundas (1997) findings were based on four patients, three of which were examined within a week time from the stroke onset. Hence, their findings might represent the phenomena of general cortical inhibition or shut-down after central nervous system (CNS) insult, where intact brain tissues are not functioning, for example due to neural shock and oedema. This inhibition is temporary and can be reversed shortly after initiation (H. Cohen, 1999).

Cingulate cortex (CC) activation was proposed to reflect the attention and/or affective component of the swallowing task during imaging (Ertekin & Aydogdu, 2003; Hamdy, Rothwell, et al., 1999; Kern et al., 1998; Kern, Jaradeh, et al., 2001; Mosier, Patel, et al., 1999; Mosier & Bereznaya, 2001). The caudal (posterior) parts of the CC were found to be involved in attention and premotor processes involved in voluntary swallowing, and the anterior CC was involved during naïve swallowing (Martin et al., 2001) implying that its activation is non-related to attentional state. In a MEG study, the anterior and posterior CC activation preceded the onset of swallowing (as measured by movement of the suprahyoid muscles) with the posterior CC activated 2.0 s before the onset of swallowing (Watanabe et al., 2004). This finding is supported by Hamdy's et al. (1999) finding of earlier activation of CC relative to other cortical areas during the 5 mL water swallow task. However, this does not help in elucidating the role of the CC since the early activation might be related to attention and/or swallowing control (Hamdy, Mikulis, et al., 1999). Another explanation of this early activation was of the anterior and posterior CC role in a cognitive process that might be required in deciding whether a bolus is ready to be swallowed (Watanabe et al., 2004).

The *SMA* is suggested to be involved in motor planning in general, and in planning sequential movements in particular (Tanji & Shima, 1996). SMA activity has been found to precede the onset of the pharyngeal swallow in studies using EEG techniques characterized by high temporal

resolution (Hiraoka, 2004; Huckabee et al., 2003). In studies using functional imaging techniques, the SMA was found to be active during the execution of swallowing tasks (Hamdy, Rothwell, et al., 1999; Martin et al., 2004; Mosier, Patel, et al., 1999). However, since functional imaging techniques like fMRI are characterized by low temporal resolution, it is possible that the SMA activity actually preceded the swallowing execution. In addition, SMA activation was detected during saliva swallowing and during imagination of saliva swallowing (Lowell et al., 2008). The same study also documented activation of cortical motor areas like M1 and the putamen during imagination of swallowing. Thus, the SMA may play a role in planning swallowing temporal sequence and activating related cortical motor areas.

Subcortical areas, such as the BG, thalamus, cerebellum, and internal capsule, have been reported to activate during volitional swallowing (Mosier & Bereznaya, 2001; Suzuki et al., 2003). Some papers reported *cerebellar* activity during capsule taking (Shibamoto, Tanaka, Fujishima, Katagiri, & Uematsu, 2007) and repetitive swallowing tasks of water (Mosier, Liu, et al., 1999; Suzuki et al., 2003; Zald & Pardo, 1999) but not during a single swallow (Kern, Birn, et al., 2001). Hence, it is suggested that the cerebellum controls the coordination, sequencing, and timing of motion (Suzuki et al., 2003; Zald & Pardo, 1999). A recent study found that TMS utilizing a paired-pulse paradigm with a conditioning pulse given over the cerebellum midline and hemispheres, and suprathreshold TMS pulse given over the pharyngeal-M1 area. The results indicated that inter-stimulus interval of 50, 100 and 200 ms was facilitatory to the pharyngeal M1, measured by greater pharyngeal MEP amplitude with shorter latency. In addition, the same study measured the effects of single-pulse stimulation over the cerebellum by assessing the MEP from pharyngeal EMG electrodes. The MEP was smaller in amplitude and had longer latency than the MEP after M1 magnetic stimulation, implying indirect activation of the pharyngeal muscles by the cerebellum (Jayasekaran, Rothwell, & Hamdy, 2011). The *BG* and *thalamus* were also found to be activated during swallowing (Mosier & Bereznaya, 2001; Suzuki et al., 2003). In a study involving principle component analysis, the BG were found to have positive correlation with the thalamus, M1, S1, and SMA but negative correlation with the cerebellum (Mosier & Bereznaya, 2001). The BG might be involved in the regulation of swallowing through inhibition and excitation of neural networks depending on input from other cortical areas (Mosier & Bereznaya, 2001; Suzuki et al., 2003).

Evidence of supranuclear control from lesions studies

Lesions studies also provide insight into central control mechanisms. Hamdy et al. (1996) used TMS to map the pharyngeal motor area in two unilateral stroke patients, one with dysphagia, and one without dysphagia. Both patients had reduced MEP responses from the affected hemisphere. However, the non-dysphagic patient had a large area of pharyngeal representation in the intact

side, whereas the dysphagic patient had a smaller area. As dysphagia was improving, the dysphagic patient showed an expansion of the pharyngeal cortical area in the intact hemisphere. In a subsequent study (Hamdy, Aziz, Rothwell, Crone, et al., 1997), MEPs were measured from the pharynx and mylohyoid muscles in 20 unilateral stroke patients, 5 of which had pharyngeal phase dysphagia, 3 oropharyngeal dysphagia and 12 were non-dysphagic. It was found that dysphagic and non-dysphagic patients had reduced MEP amplitude from the pharyngeal muscles when TMS was applied on the affected hemisphere, with no differences in amplitude between the groups. However, when measuring the non-affected side, dysphagic patients had smaller responses from the pharyngeal M1 than non-dysphagic. The conclusion was that the pharyngeal and oesophageal muscles had unilateral hemispheric representation, indicating the existence of a dominant hemisphere. In contrast, the mylohyoid muscle was represented symmetrically bilaterally and the MEP response did not differ between dysphagic and non-dysphagic when measuring the non-affected hemisphere (Hamdy et al., 1996; Hamdy, Aziz, Rothwell, Crone, et al., 1997). Lack of differences between dysphagic and non-dysphagic in mylohyoid excitability might be due to the fact that MEPs were collected during rest, and it is possible that although mylohyoid representation remained the same, its function during swallowing might have been impaired. Alternatively, since 5/8 had pharyngeal dysphagia and 3/8 had oropharyngeal dysphagia, it is possible that mylohyoid MEPs were reduced among those with oral phase involvement but due to low participant number, this reduction was not significant. In another study by the same group (Hamdy, Aziz, et al., 1998), the recovery course of unilateral stroke patients with pharyngeal phase dysphagia was assessed. Of those who presented with dysphagia and recovered, an increase in the area representing the pharyngeal muscles in the intact hemisphere was documented with no change in the affected hemisphere. In those who did not recover, no change was demonstrated in pharyngeal representation in either hemisphere. The conclusion of Hamdy and colleagues (Hamdy et al., 1996; Hamdy, Aziz, Rothwell, Crone, et al., 1997; Hamdy, Aziz, et al., 1998; Hamdy & Rothwell, 1998) was that pharyngeal control was asymmetrically represented so that one hemisphere was dominant in its motor control. This dominance, much like speech control dominance in the left hemisphere, may predispose a patient to become dysphagic subsequent to a stroke. However, the dominant hemisphere varied among people, unlike speech dominance, which is usually on the left. If the dominant hemisphere for swallowing was damaged, the non-dominant hemisphere could not gain control of pharyngeal function. This would imply that pharyngeal phase dysphagia recovery is dependent on restoring the function of the affected hemisphere. Hamdy et al.'s studies demonstrated that dysphagia can occur immediately at stroke onset, even if the insult is in the non-dominant hemisphere for pharyngeal swallowing. This might be due to the bilateral innervation of the muscles involved in swallowing. Although contralateral innervation was demonstrated to be greater than ipsilateral, an insult can affect the existing balance in neural

innervation. Plastic changes following stroke can develop over time and may allow the dominant hemisphere to solely control swallowing (Hamdy, Aziz, et al., 1998).

In a different study that documented the recovery of tongue muscle paralysis following unilateral stroke, 5/6 patients demonstrated increased control of the intact hemisphere over the ipsilateral tongue muscles associated with recovery of the muscles. In those five patients, the affected hemisphere remained unchanged throughout the course of recovery with no compound muscle action potential response. The unaffected hemisphere showed increased control over the ipsilateral side, taking over the role of the affected side. The amplitude from ipsilateral tongue muscles, before tongue recovery was half the size of the contralateral response. Post recovery, the amplitude of the ipsilateral motor response doubled in amplitude, and was similar to that recorded from the contralateral side. The authors concluded that, for midline muscles like the tongue that are innervated bilaterally, the intact hemisphere is the one responsible for recovery. However, it is important to clarify that although tongue paralysis was present, dysphagia was not reported or assessed. It is not clear if functional recovery, for speech or swallowing for example, was accompanying the muscular recovery and neural changes documented. The authors suggested that injury to one hemisphere likely activates uncrossed, unilateral pathways, leading to functional gains (Muellbacher et al., 1999). Presuming that Hamdy's suggestion regarding unilateral control over the pharynx is correct, this mechanism of recovery, by which the affected hemisphere increases its neural control over the unilateral musculature, is less likely to take place.

To summarize, many supranuclear area are activated before and/or during swallowing with M1, S1, insula, SMA, cingulate cortex, cerebellum and BG included. Electrical stimulation of face-M1 and stimulation of the white matter and frontal operculum elicited a pharyngeal swallow in primates (Martin et al., 1999). Thus, it is possible that the cortex contains sites that control swallowing initiation. Using TMS, corticobulbar projections from different M1 sites were found to elicit a response in the submental, pharyngeal and oesophageal muscles. The mylohyoid muscles are bilaterally and symmetrically represented, whereas the pharyngeal and oesophageal muscles are bilaterally but asymmetrically represented. The asymmetry could be to the right or left sides, regardless of handedness (Hamdy et al., 1996; Hamdy, Aziz, Rothwell, Crone, et al., 1997). Since the muscles that participate in swallowing, take part in other motor activities, M1 control changes according the task, ranging from bilateral innervation to unilateral. S1 is likely to be involved in processing sensory information. Neural activity of the SMA, insula, and CC was reported to precede swallowing execution; however their role in swallowing is still not clear. The insula might be related to processing taste sensation. The posterior CC might be related to attention to the task, and the anterior CC might be related to swallowing control. The SMA was found to be active during imagination of saliva swallowing and actual swallowing. This might

support its role in planning the temporal sequence of swallowing. The cerebellum was found to be activated during more complex swallowing tasks like repetitive swallowing. This can indicate that it may be involved in coordination of swallowing.

Lack of recovery of pharyngeal phase dysphagia was associated with damage to the dominant hemisphere for pharyngeal control (Hamdy, Aziz, et al., 1998). The recovery course of swallowing is different from recovery for limbs, either due to the bilateral innervation of the swallowing muscles or due to possible hemispheric dominance over swallowing. Gaining more information regarding supranuclear control over swallowing would help to develop better rehabilitation programmes.

2.3 Dysphagia

2.3.1 Definitions

Swallowing disorders or impairments (dysphagia) are characterized by disruption of the precise activation-patterns of nerves and/or muscular execution, which ultimately effects functional bolus flow. Logemann defined dysphagia as a condition characterized by difficulties transferring the bolus from the mouth to the stomach due to difficulties with awareness during feeding, visual and olfactory recognition of the bolus and its presence, difficulties in pre-motor acts in preparation of the food and/ or difficulties with motor acts during swallowing (Logemann, 1998).

Impairments or interruptions can occur in one or more of the processes involved in the execution of swallowing (Perlman & Schulze-Delrieu, 1996). At the beginning of this chapter, the phases of swallowing were discussed in the context of normal swallowing, but the same phases can be used in describing specific impairments (Daniels & Huckabee, 2008; Perlman & Schulze-Delrieu, 1996). Thus, impairment can occur in the pre-oral phase, oral preparatory stage, oral propulsive or transit stage, pharyngeal phase and/or oesophageal phase (Daniels & Huckabee, 2008; Leopold & Kagel, 1997; Perlman & Schulze-Delrieu, 1996).

Difficulties during the oral phase of swallowing can be secondary to decreased control and decreased ability to manipulate and prepare a bolus for swallowing. These difficulties can result in bolus leakage from the anterior oral cavity, premature spillage of the bolus from the oral cavity to the pharynx leading to penetration or aspiration. Difficulties during the oral transit phase can be due to delayed initiation of the pharyngeal swallow following bolus transfer to the pharynx, and can lead to penetration or aspiration of the bolus (Perlman & Schulze-Delrieu, 1996). The pre-oral and oral stages have an important role in sensory perception of the bolus characteristics and are

important for providing sufficient sensory input to the brainstem CPG for motor planning of the pharyngeal swallowing response (Daniels & Huckabee, 2008). Due to the complexity of the pharyngeal phase, with high levels of coordination and inter-relationships between events, even minor disruptions can lead to dysphagia (Feinberg & Ekberg, 1991). Incomplete velopharyngeal closure can lead to decreased pharyngeal pressure. Decreased base of tongue approximation to the posterior pharyngeal wall can lead to penetration or aspiration of pharyngeal residuals. Inadequate hyolaryngeal excursion can have extensive effects on swallowing biomechanics, including decreased epiglottic deflection, which will result in decreased airway protection and vallecular residuals. In addition, inadequate excursion can result in decreased opening of the UES leading to pharyngeal residuals at the pyriform sinuses, and thus, increased risk for residuals aspiration (Daniels & Huckabee, 2008; Perlman & Schulze-Delrieu, 1996). Both oral phase and pharyngeal phase dysphagia can lead to aspiration. In a study of 50 patients with aspiration due to dysphagia, 46% had oral phase dysphagia, 20% had pharyngeal phase dysphagia, and 34% had dysphagia in both phases (Feinberg & Ekberg, 1991).

2.3.2 Complications of dysphagia

From the patients' perspective, dysphagic symptoms can include the feeling of the bolus “sticking or holding up... in the neck” (Cook, 2008, p. 394), and complaints of “something went down the wrong way” (Jafari, Prince, Kim, & Paydarfar, 2003, p. 292). Additional complaints may include reports on presence of hiccups, pain or pressure in the throat, chest discomfort or pain, bolus regurgitation, and inability to consume food or drinks, and even saliva (Cook, 2008; Perlman & Schulze-Delrieu, 1996). Coughing before, during, or after eating or drinking can be reported as well. In severe cases, the airways can be blocked by the bolus and breathing is restricted. Wet voice can become apparent (Perlman & Schulze-Delrieu, 1996).

Dysphagia can interfere with medical recovery leading to longer hospitalization and long-term care (Odderson, Keaton, & McKenna, 1995). The most common health complications of dysphagia are aspiration pneumonia, malnutrition and dehydration (Schindler, Ginocchio, & Ruoppolo, 2008). Aspiration of saliva containing colonization of pathogenic bacteria from the oropharynx can lead to pulmonary infection (Langmore et al., 1998; Marik & Kaplan, 2003), which is associated with high morbidity, mortality, and cost (Baine, Yu, & Summe, 2001; Niederman, 1998). An epidemiological study conducted between 1991 and 1998, sampled 5% of patients over 65 who had been hospitalized due to pneumonia in the United States (as reported by the United States Department of Health and Human Services). Of these, 3.3% were diagnosed with aspiration pneumonia in 1991 and this had increased to 5.3% in 1998 (Baine et al., 2001). The authors suggested that this increase might be secondary to increased genetic and

environmental risk factors, and possibly increased occurrence of co-morbidities resulting in aspiration pneumonia. Swallowing difficulties do not only pose a physical problem but also have social and psychological impact. Ekberg, Hamdy, Woisard, Wuttge-Hannig, & Ortega (2002) reported increased anxiety and panic during meals and avoidance from social eating.

2.3.3 Prevalence of dysphagia in the general population

In the United States, approximately 18 million adults have dysphagia (Robbins et al., 2008). In a study by Wilkins, Gillies, Thomas, & Wagner (2007), self-report questionnaires were filled by adults over 18 years who attended primary care practice sites in the United States. The study revealed that 26.6% (214) of 947 participants reported having dysphagia symptoms several times per month. In a similar study in Australia, self-report questionnaires were randomly posted to 1000 adults above 18, and revealed that 16% of the responders (110/672) reported dysphagia events at some point in their lives (Eslick & Talley, 2008). The difference in the prevalence of dysphagia between the two studies might be due to unequal representation of gender in the Wilkins et al. (2007) study, and equal representation in the Australian study. As Wilkins et al. (2007) postulate, women are more likely to report difficulties than men. In addition, it is possible that due to differences in sampling methods, the two studies included different populations. The U.S. study might have included more people who were aware of symptoms affecting their health, as the questionnaires were filled in a medical facility. In contrast, the Australian study might have included people with reduced awareness to swallowing difficulties, as the questionnaires were randomly posted. Nearly half of those who reported on dysphagia did not discuss it with their physician, although dysphagia did affect their eating behaviours, including social eating and use of strategies during mealtime (Wilkins et al., 2007). This might be a matter of low availability of services that can aid with management of dysphagia, or a lack of awareness of services. Prevalence of dysphagia in specific populations will be reported below.

2.3.4 Aetiology of dysphagia

Dysphagia can result from a broad spectrum of acquired health conditions, including cerebrovascular accident (stroke), traumatic brain injury, head and neck cancer, and neurodegenerative diseases like Parkinson's disease (PD) and Huntington's disease. It may also occur as a result of prematurity and developmental disability, including cerebral palsy. Acquired health conditions that cause dysphagia can be further divided into neurogenic and structural causes, but the prevalence distribution is not even and most cases of chronic dysphagia are from neurogenic causes (Perlman & Schulze-Delrieu, 1996).

2.3.4.1 *Neurogenic dysphagia*

Different aetiologies can lead to neurogenic dysphagia, but a common result is sensorimotor impairment that disrupts muscle action (Perlman & Schulze-Delrieu, 1996). Hence, during intervention and management, the underlying cause needs to be taken into account (Perlman & Schulze-Delrieu, 1996). The development of symptoms varies with aetiology: rapid onset in stroke versus slow deterioration in amyotrophic lateral sclerosis, fluctuations in myasthenia gravis (MG), and relapses and remission cycle in multiple sclerosis (MS) (Perlman & Schulze-Delrieu, 1996). Different symptoms can indicate the location of the insult in the brain. LMN damage includes damage to the CN nuclei in the medulla and pons, the CN, the muscle fibres, and the neuromuscular junctions. LMN damage can result in weakness, reduced tone, muscle atrophy, paralysis, and decreased reflexes. UMN damage includes damage to the neurons of the pyramidal or extrapyramidal tract, and will manifest as incoordination, weakness, hypertonicity, impairment of voluntary actions execution, and increased reflexes (Perlman & Schulze-Delrieu, 1996). UMN damage located prior to pyramid decussation will result in contralateral damage whereas damage located after the decussation, will result in ipsilateral damage (Fix, 2008). Bulbar (*bulb* is a term for the medulla oblongata, although nowadays it also refers to the pons) insult will involve the LMNs or the UMNs, depending on site of lesion. A pseudobulbar insult will affect UMNs (Perlman & Schulze-Delrieu, 1996). The most common complications of neurogenic dysphagia are dehydration, malnutrition, and aspiration pneumonia, which can lead to long hospitalization and death (Baine et al., 2001; Niederman, 1998).

2.3.4.1.1 *Stroke*

Approximately 60,000 New Zealanders are living with the consequences of stroke (Ministry of Health, 2008). According to the World Health Organization (WHO) report, the incidence of stroke is approximately 200 cases per 100,000 people (Soler & Ruiz, 2010). Since stroke is more prevalent in older people, when examining the incidence of stroke among people above the age of 55 the incidence was 420–650 cases per 100,000 people, depending on the country. Stroke is the most common cause of dysphagia (Kuhlemeier & Stiens, 1994) and up to 70% of stroke patients will present with dysphagia (Marik & Kaplan, 2003). Forty to 50% of stroke patients with dysphagia will have aspiration and are at a higher risk for pneumonia (Horner, Massey, Riski, Lathrop, & Chase, 1988; Marik & Kaplan, 2003).

Looking closely into types of stroke and their influence on dysphagia, brainstem stroke and mixed stroke (brainstem and hemispheric) are more likely to result in dysphagia than hemispheric stroke (Lorish, Sandin, Roth, & Noll, 1994), with 39-40% incidence for hemispheric lesions, 51-55% for

mixed lesions (Martino et al., 2005), and 40-81% for specific brainstem stroke (Chua & Kong, 1996; Meng, Wang, & Lien, 2000; Teasell, Foley, Fisher, & Finestone, 2002). However, brainstem stroke is less common in occurrence than stroke in other brain areas, and only 15% of all patients admitted to stroke rehabilitation units had an aetiology of brainstem stroke (Kruger, Teasell, Salter, Foley, & Hellings, 2007). In addition, stroke affecting other subcortical locations such as the basal ganglia and the cerebellum can also lead to dysphagia (Langdon, Lee, & Binns, 2007).

Brainstem lesions can affect muscles of the face and pharynx and also the coordinated and precise movement required for triggering the pharyngeal swallow, laryngeal elevation, airway protection and UES opening (Martino et al., 2001; Veis & Logemann, 1985). Since the brainstem contains dense packaging of CNs, sensory and motor nuclei, and reticular interneurons that comprise the CPG for swallowing, brainstem damage often has severe consequences and there is a lower chance for spontaneous recovery in comparison to hemispheric stroke. However, recovery is possible as Chua & Kong (1996) reported. Fifty three patients with brainstem stroke dysphagia who were tube fed went through intensive treatment in an inpatient rehabilitation institution and only 6 of them required tube feeding on discharge.

Unilateral or bilateral hemispheric stroke can result in dysphagia in 39% (Parker et al., 2004) to 71% (Hamdy, Aziz, et al., 1998) of cases. One of the reasons for this wide range is the time of investigation relative to the onset of the stroke. The high occurrence rate reported by Hamdy et al. (1998) dropped from 71% to 40% at 3 month post onset indicating spontaneous recovery from dysphagia, whereas in brainstem stroke effects tend to last longer and the high incidence of dysphagia post-onset confirms that (Chua & Kong, 1996; Martino et al., 2005). Unilateral hemispheric lesions can impair contralateral muscles of the face and pharynx (Martin & Sessle, 1993; Veis & Logemann, 1985). Although most of the swallowing muscles are bilaterally innervated, the ipsilateral projections of the intact hemisphere are not as strong as the contralateral projections (Muellbacher, Artner, & Mamoli, 1999). In addition there is support in the literature for hemispheric dominance of pharyngeal control (Hamdy, Aziz, et al., 1998). Bilateral lesions affect muscles on both sides and increase the likelihood of aspiration (Horner et al., 1988).

Cerebral stroke can cause impairments in the oral phase due to its contribution to innervation during mastication and bolus transport (Daniels, Brailey, & Foundas, 1999; Martin & Sessle, 1993; Zald & Pardo, 1999). Adverse effects on the pharyngeal phase have been documented as well (Hamdy, Aziz, Rothwell, Crone, et al., 1997; Hamdy, Aziz, et al., 1998; Robbins & Levin, 1988). In addition, cognitive function might be impaired following hemispheric stroke which may lead to oral preparatory stages difficulties due to decreased bolus recognition and attention (Parker et al., 2004). Insults to the left hemisphere were found to be related to oral phase dysphagia

including difficulty initiating coordinated oral movements, apraxia, and longer pharyngeal transit durations. Insults to the right hemisphere were related to pharyngeal stage impairment, such as pharyngeal pooling, longer pharyngeal stage durations, and higher incidences of laryngeal penetration and aspiration of liquid (Robbins & Levin, 1988; Robbins, Levine, Maser, Rosenbek, & Kempster, 1993). However, there are disagreements between studies that suggested an associative link between lesion location and symptoms. While some suggest a link between the side of the hemispheric lesion and the presence of aspiration, with right-sided lesions associated with aspiration (Robbins & Levin, 1988; Robbins et al., 1993), another study suggests no link between the two (Alberts, Horner, Gray, & Brazier, 1992). Yet, another suggests a different link that relates anterior, rather than posterior, location of the lesion to be associated with aspiration (Daniels & Foundas, 1999). Dysphagia following stroke can recover spontaneously, but there is evidence for persistent dysphagia among some patients even at 6 month post stroke (Mann, Hankey, & Cameron, 1999).

2.3.4.1.2 *Iatrogenic factors form surgery*

Head, neck, and neurological surgery can result in dysphagia due to intraoperative damage. Neck surgery can cause pharyngeal plexus denervation leading to dysphagia due to the important role of this CN grouping during the oral and pharyngeal phases. Posterior fossa surgery can result in vascular compromise of the brainstem structures and CNs resulting in dysphagia (Perlman & Schulze-Delrieu, 1996). Following surgery at the cerebellopontine angle, 31% patients present with dysphagia (Starmer et al., 2012). Dysphagia subsequent to cerebellopontine angle resection may present similarly to dysphagia secondary to stroke since damage can affect the UMN and/or the LMN.

2.3.4.1.3 *Degenerative diseases*

Degenerative diseases of the CNS are often characterized by the presence of neurogenic dysphagia (Perlman & Schulze-Delrieu, 1996).

Parkinson's disease

Dysphagia in patients with PD ranges from 18% (Mutch, Strudwick, Roy, & Downie, 1986) to 95% (Nagaya, Kachi, Yamada, & Igata, 1998; Wintzen, Badrising, Roos, Vielvoye, Liauw, et al., 1994). Dysphagia was reported for oral, oral transit, pharyngeal and oesophageal phases (Johnston, Li, Castell, & Castell, 1995; Leopold & Kagel, 1997; Nagaya et al., 1998). See Section 8.2 - *Literature Review*, for details regarding dysphagia characteristics and dysphagia management in PD.

Multiple sclerosis

Thirty three to 43% of patients with MS have dysphagia (Hartelius & Svensson, 1994; Merson & Rolnick, 1998; F. J. Thomas & Wiles, 1999), with higher prevalence in those who have brainstem involvement (Calcagno, Ruoppolo, Grasso, De Vincentiis, & Paolucci, 2002). Dysphagia is present among mildly impaired MS patients and its prevalence increases as the disease severity increase, with 95% prevalence among the most severe cases. MS patients with mild severity presented oral phase dysphagia, and involvement of the pharyngeal phase was apparent among those with more severe rating of disability (De Pauw, Dejaeger, D'hooghe, & Carton, 2002).

Dementia

It has been estimated that 45% of institutionalized patients with dementia have some type of dysphagia (Horner, Alberts, Dawson, & Cook, 1994). Alzheimer's disease is the most common form of dementia and accounts for more than half of all dementia cases (Breteler, Claus, van Duijn, Launer, & Hofman, 1992). Horner et al. (1994) used VFSS and found that dysphagia is common in individuals with Alzheimer's disease, with symptoms appearing in 21 of 25 patients. The most common symptoms include prolonged oral phase, delayed pharyngeal swallow and inefficient pharyngeal clearing that lead to inconsistent airway protection (Priefer & Robbins, 1997). In addition, holding food in the mouth, poor lingual control (Chouinard, Lavigne, & Villeneuve, 1998) and decreased chewing (Priefer & Robbins, 1997) were also documented. Like in other neurodegenerative diseases, there was a positive correlation between the severity of the dementia and dysphagia severity, and in the late disease stage, dysphagia and aspiration pneumonia are the most serious complications leading to death (Kalia, 2003).

Huntington's disease

Huntington's disease, a hereditary degenerative disease of the BG, is commonly accompanied by dysphagia of the oral and pharyngeal phases. Some symptoms include lingual and laryngeal chorea, swallow incoordination, repetitive swallows, prolonged laryngeal elevation, pharyngeal residue, and aspiration, which often leads to aspiration pneumonia and its complications including mortality (Kagel & Leopold, 1992).

Myasthenia gravis

MG is an autoimmune disease that results in weakness of skeletal muscles. Specifically related to swallowing, MG patients also show weakness of labial, mandibular, lingual, velopharyngeal and pharyngeal muscles, thus leading to impairments in the oral and pharyngeal phases. Colton-Hudson et al. (2002) documented delayed onset of laryngeal elevation and epiglottic deflection

resulting in decreased airway protection, decreased glossopalatal seal leading to premature spillage into the pharynx, decreased tongue base retraction toward the pharyngeal wall and decreased elevation of the larynx that increase pharyngeal residuals and can increase the risk of aspiration. Aspiration pneumonia is a significant source of morbidity and mortality in MG (C. E. Thomas et al., 1997).

2.3.4.1.4 *Traumatic brain injury*

Traumatic brain injury (TBI) may damage the cerebral cortex or subcortical areas including the brainstem and CNs. Thus, head trauma can result in dysphagia, similar to the consequences of stroke (Perlman & Schulze-Delrieu, 1996).

2.3.4.1.5 *Mental illnesses*

Among people with mental illnesses the prevalence of dysphagia ranges between 9% to 46% (Aldridge & Taylor, 2012). Patients with organic mental disorder resulting from cerebral dysfunction are 43 times more likely to die from airway obstruction than the general population (Ruschena et al., 2003).

2.3.4.2 *Head and neck tumours*

Dysphagia can also be a consequence of structural deficiencies. The treatment of head and neck tumours can cause greater dysphagia than that of the original tumour (Perlman & Schulze-Delrieu, 1996). The site and size of the lesion, type of treatment, and in case of a surgery, the degree of surgical resection, types of structures resected, and type of reconstruction will all determine the degree of dysphagia post treatment (Pauloski, 2008). Lesions can appear on the palate, buccal mucosa, mandible, tongue, pharynx, larynx, or oesophagus. Treatment can include surgery, radiotherapy, and/or chemo-radiotherapy with adverse side effects of sensory and motor denervation (Pauloski, 2008). Resection of oropharyngeal structures used for bolus formation, bolus transit, and airway protection such as oral tongue, tongue base, or arytenoid cartilages will impact swallowing. Resection of the oral tongue will result in difficulty with bolus formation, slow oral transit, and increased oral residue. Resection of the tongue base can increase oral preparatory time, oral transit time and increase oral and pharyngeal residue (Borggreven et al., 2007; Hirano et al., 1992; Zuydam, Rogers, Brown, Vaughan, & Magennis, 2000). Resection of greater than 25% of the tongue base is associated with inability to trigger a pharyngeal swallow, difficulty clearing the bolus from the pharynx, and severe postsurgical aspiration. Laryngeal resections can have profound impact on swallowing function, and increase the risk of aspiration (Pauloski, 2008). Chemo-radiotherapy can result in fibrosis and limitations of movement of the

oropharyngeal structures, and can also cause reduction in salivary flow and xerostomia. Other common side effects can be injury to the oral mucosa, oral mucositis, characterized by erythema (redness), ulcerative lesions in the oral cavity, and stricture, segmental narrowing or closure of the pharynx or oesophagus (Pauloski, 2008). Dysphagia management includes the use of prosthetics, compensatory techniques, and rehabilitation exercises (Perlman & Schulze-Delrieu, 1996).

2.3.4.3 *Age*

Dysphagic symptoms become more prevalent with increased age and, more specifically, above the age of 60 years (Shaw, 1981). The prevalence of dysphagia is estimated at 16-22% among people 55 years and above (Kuhlemeier, 1994), but among those in resting homes, the prevalence increases to approximately 50% (Bloem et al., 1990; Robbins et al., 1992).

Due to the increased prevalence, a question arises as to whether dysphagia is a consequence of aging per se or a consequence of an age-related disease (Perlman & Schulze-Delrieu, 1996; Sonies, 1992). It is known that there is a decline in skeletal muscle strength related to reduced muscle mass above the age of 60 years (Evans, 1995). Thus, there are physiological reasons to expect age-related changes in swallowing muscles as well. Indeed, non-dysphagic elderly were documented to show changes in swallowing physiology (Logemann et al., 2000; Robbins et al., 1992). Oral phase difficulties have been reported and included decreased tongue pressure during bolus transit (Robbins, Levine, Wood, Roecker, & Luschei, 1995), decreased isometric tongue pressure (Nicosia et al., 2000), together with decreased ability to manipulate the bolus due to loss of teeth (Chauncey et al 1984), decreased saliva production (Gilbert, Heft, & Duncan, 1993), and slowness during oral phase processing (Logemann, 1990). Slowness during bolus transit, delayed pharyngeal swallow, and reduced UES opening were reported as well (Logemann, 1990). In addition, progressive decreases in sensitivity of the pharynx and supraglottic area were documented with advances in age (Aviv et al., 1994), which might explain the prevalence of aspiration among 38% of community-dwelling healthy elderly between the age of 60-90 years (Butler et al., 2011). Although changes in swallowing function have been reported, it is important to remember that changes in swallowing do not necessarily translate into dysphagia. Elderly individuals can stay asymptomatic and continue to eat their normal diet safely (Robbins et al., 1992; J. F. Tracy et al., 1989).

2.3.5 *Dysphagia management*

There is a paucity of evidence in the literature regarding dysphagia management (Bath, Bath, & Smithard, 2000; Hamdy et al., 2003; Singh & Hamdy, 2006). In the past, the aim of dysphagia management was primarily to prevent aspiration pneumonia (Daniels & Huckabee, 2008).

However, there has been a change towards increased emphasis on rehabilitation to induce long-term effects on swallowing function.

Dysphagia management can be broadly divided into compensation and rehabilitation strategies (Daniels & Huckabee, 2008; Singh & Hamdy, 2006). Compensatory techniques aim to allow safe feeding, without compromising the airways, and to maintain adequate nutritional status, which was found to predict the length of hospital stay and functional outcomes (Finestone, Greene-Finestone, Wilson, & Teasell, 1996). These techniques influence swallowing only during the moment of implementation without having any long-term effects or carry-over. These techniques include diet modifications like increasing the bolus consistency or changing bolus size, postural changes like head turn and chin tuck, and breath holding techniques like supra-glottic swallow (Daniels & Huckabee, 2008). Daniels & Huckabee (2008) describe the use of compensatory techniques as a temporary solution to enable oral intake, followed by rehabilitation intervention if dysphagia has not spontaneously recovered. Another type of compensatory intervention includes alternative feeding (Bine, Frank, & McDade, 1995) by nasogastric tube, or percutaneous endoscopic gastrostomy. In a large randomized controlled trial, nasogastric tubes were found to improve survival rates in stroke patients with dysphagia (M. Dennis, Lewis, Cranswick, & Forbes, 2006), whereas percutaneous endoscopic gastrostomy increased the risk of death (Dennis, Lewis, & Warlow, 2005). In addition, research has shown that risk of aspiration pneumonia remains in the presence of alternative feeding (M. S. Dennis et al., 2005; Finucane & Bynum, 1996), since poor dentition and oral care can still be present and lead to colonisation of bacteria which can be aspirated to the lungs due to reduced ability to manage secretions (Langmore et al., 1998).

Rehabilitation techniques are used to facilitate recovery (Singh & Hamdy, 2006), and should have long-lasting effects. Rehabilitation techniques can be further divided into 3 groups: (1) exercises that involve swallowing, including effortful swallow and tongue hold manoeuvre; (2) swallowing-related exercises that do not involve swallowing, such as head-lift and oral motor exercise; (3) and non-swallowing-related exercises that indirectly influence swallowing, such as expiratory muscle strength training (EMST). In addition to, but different from non-swallowing-related exercises, Lee Silverman voice therapy (LSVT) can result in some improvement in oral-phase dysphagia, due to a generalized affect on the integrated oropharyngeal mechanism, although it is important to emphasize that LSVT is not prescribed to patients as a swallowing rehabilitation technique. These are all motor exercises that, generally speaking, aim to increase strength. In addition, sensory-stimulation techniques have been proposed in the literature and aim to increase the sensory component, for example tactile and thermal stimulation (Rosenbek et al., 1998) and low-threshold electric stimulation (Fraser et al., 2002).

Most of the literature regarding dysphagia management focuses on either compensatory techniques or the immediate effects of swallowing manoeuvres. For example, most of the current management techniques for dysphagia among people with MS focus on dietary modifications and use of compensatory techniques like supra-glottic swallow (Giusti & Giambuzzi, 2008). Due to the nature of this disease, strenuous exercise might exacerbate symptoms, although this is a controversial issue (Dalgas, 2011). There is limited research on swallowing rehabilitation in MS and the effects of strength training are still not clear (De Pauw et al., 2002). Dysphagia management in people with dementia includes cuing techniques to increase awareness and compensatory techniques, but these require adequate cognitive ability to follow verbal instructions to perform the swallowing manoeuvre (Easterling & Robbins, 2008). Dysphagia management in Huntington's disease also consists on compensatory techniques (Heemskerk & Roos, 2011). Dysphagia management for people with MG include compensatory strategies such as diet modification, behavioural techniques, postural techniques, and non-oral feeding. Strength exercises are not recommended due to muscles fatigue (Colton-Hudson et al., 2002). Management of dysphagia in people with TBI might be further complicated due to the presence of cognitive and behavioural impairments (Alhashemi, 2010; Perlman & Schulze-Delrieu, 1996). Hence, it is possible that using approaches that increase awareness of motor acts, such as biofeedback based approaches, might have beneficial results. The topic of dysphagia rehabilitation is discussed further in Section 3.1.2 *Strength training in swallowing rehabilitation*.

2.3.6 Summary: Dysphagia aetiology and management

Dysphagia can result from neurological or structural aetiologies, with the most common condition being stroke (Perlman & Schulze-Delrieu, 1996). Compensatory techniques improve bolus flow, thereby facilitating airway protection. These techniques provide a temporary solution to dysphagia, for example immediately after stroke. In degenerative conditions such as Huntington's disease and dementia, compensatory techniques may serve as a long-term solution. Rehabilitation techniques facilitate recovery and include exercises that should have long lasting effects. There is a need to develop specific rehabilitation programmes, as the pathophysiological basis is different between conditions.

2.4 Measuring change following swallowing-related behavioural intervention

In 2007 and 2008, several papers were published in the area of translational research in speech in language sciences, including swallowing research. An action plan for research was created and

included motor learning and neural plasticity principles that are relevant to research in communication disorders. In order to translate these principles from basic science into clinical practice, there is a need to test their application in communication disorders research (Burkhead, Sapienza, & Rosenbek, 2007; Gonzalez Rothi et al., 2008; Ludlow et al., 2008; Robbins et al., 2008). Logemann (2005) discussed the need for systematic evaluation of swallowing intervention. She specifically mentioned the importance of foundation research in evaluating neuromuscular adaptation among normal subjects in response to swallowing exercises. Information regarding neuromuscular adaptations can contribute to planning treatment programmes for dysphagia, and to creating appropriate methods for assessing efficacy (improvement resulting from a treatment as measured in research) and later efficiency (improvement resulting from a treatment applied in the clinic) (Rosenbek, 1995).

In order to understand the specific influence of various treatment parameters, changes should be measured at different levels of the neuromuscular system. Assessment at the neural level is important since studies have shown differences in excitability when comparing skill- to strength-training approaches (Jensen, Marstrand, & Nielsen, 2005). The muscular level should be measured, since motor activity has been shown to cause changes in muscles size (Robbins et al., 2005, 2007), and changes in the recruitment pattern of muscles (Van Cutsem, Duchateau, & Hainaut, 1998). Measurements of the biomechanical level should also be included, since changes in muscle activity pattern and muscle size influence activation trajectory (Clark, 2003; Luschei, 1991; Wheeler-Hegland, Rosenbek, & Sapienza, 2008). In addition, the task performance level should be assessed for changes in response to different training programmes (Jensen et al., 2005). The following sections include discussion of neurophysiological, biomechanical, and structural assessment tools.

2.4.1 Measuring neurophysiological changes

Neural assessment techniques

Improvements in measuring the neural substrates of swallowing have answered an emerging need for evidence-based approaches in dysphagia rehabilitation that included documentation of neural changes (Ludlow et al., 2008; Robbins et al., 2008). Several functional neuro-imaging techniques have been used in swallowing research to assess brain function associated with swallowing and swallowing-related behaviours, among them are fMRI (Humbert et al., 2009; Kern, Jaradeh, et al., 2001; Martin et al., 2001; Suzuki et al., 2003; Toogood et al., 2005; Zald & Pardo, 1999), PET (Hamdy, Rothwell, et al., 1999), MEG (Teismann et al., 2009), and EEG (Huckabee et al., 2003). Of these, fMRI had been the most widely used technique in swallowing research to document

brain activation during different swallowing tasks as reported before in Section 2.2.4 *Supranuclear control of swallowing*. However, it has not been used to document changes in brain activation as a result of swallowing-related intervention. In addition, fMRI is a relatively expensive technique which requires the subjects to swallow while lying supine (Martin et al., 2001). Its methods can introduce difficulties for older people during swallowing tasks since there is a conflict between the acquisition time that should be kept relatively short in order to reduce costs and the extended time required by elders to volitionally generate enough saliva for swallowing (Bergdahl, 2000; Martin et al., 2007).

TMS has been widely used to document learning-dependent changes following skill training of the limbs (Jensen et al., 2005; Pascual-Leone et al., 1995; Pearce, Thickbroom, Byrnes, & Mastaglia, 2000). It had also been used to document changes in excitability in M1 as a result of natural recovery of swallowing following stroke (Hamdy, Aziz, Rothwell, Crone, et al., 1997; Hamdy, Aziz, et al., 1998), so as to document changes in excitability in M1 following implementation of an effortful-swallowing protocol among healthy adults (Macrae, 2011) and a tongue protrusion task (Svensson, Romaniello, Arendt-Nielsen, & Sessle, 2003; Svensson, Romaniello, Wang, Arendt-Nielsen, & Sessle, 2006). Thus, single-pulse TMS has the capacity to capture changes in excitability as a result of neural recovery or intervention.

Use of TMS for neurophysiological assessment

TMS is a non-invasive, safe, painless and relatively inexpensive technique (Kapogiannis & Wassermann, 2008). It was first introduced in 1985 as a technique for stimulating the motor cortex in humans (Barker, Jalinous, & Freeston, 1985) and offered a better tolerated alternative to transcranial electrical stimulation (TES) in order to elicit MEPs (Hallett, 2000). Magnetic stimulation produces magnetic fields that pass through high resistance structures (like the skull) with no pain (Barker et al., 1985), as opposed to TES that causes considerable discomfort (Merton, Hill, Morton, & Marsden, 1982). Specific to the primary motor cortex and in comparison to fMRI, TMS is a tool for measuring the output of the motor cortex activity whereas fMRI is a technique for measuring the intracortical processing associated with the motor task (Wassermann, Epstein, & Ziemann, 2008).

TMS is frequently used in research to measure brain physiology (Hallett, 2000). The use of TMS is based on a theoretical concept by which neurons can be externally excited by electromagnetic fields that have certain characteristics (see discussion below in this section). Changes in the excitability of the primary motor cortex following intervention are based on the evoked motor response, which can be quantified. The assumption is that a greater motor response to TMS stimulation indicates greater excitability of excitatory interneurons or reduced excitability of the

inhibitory interneurons, greater number of recruited motor neurons, and other factors to be discussed (*Factors influencing the MEP magnitude*) (Wassermann et al., 2008). This is inferred from findings documenting recovery after stroke that indicated diminished MEP response immediately following stroke, but with spontaneous recovery, increased MEP responses appeared concurrently with increased swallowing function (Hamdy, Aziz, et al., 1998). It is plausible that swallowing intervention for neurological dysphagia would result in increase motor evoked response. This leads to a discussion regarding two main topics: TMS characteristics and their influence on the neurons (biophysics of TMS), and the characteristics of the motor evoked response or potential.

Biophysics of TMS

Single-pulse TMS can measure neural excitability in response to the induced magnetic pulse over the cortex. TMS is based on principles of electromagnetic induction that produce currents with sufficient magnitude to depolarize neurons (Wagner, Valero-Cabre, & Pascual-Leone, 2007). The first principle is Ampere's law, according to which a magnetic field will be induced as a consequence of electric currents flowing through a conductor. In TMS, the magnetic coil is connected to an electrical capacitance, which is an energy storage unit. The capacitor is charged with a high voltage which is required to generate a strong magnetic field (measured in Tesla) in the magnetic coil (Walsh & Pascual-Leone, 2003). The electrical capacitor discharges a very high electric current (~10,000 A) through the magnetic coil. This electric current that runs through the coil (Figure 2.5 - left), produces a magnetic field with lines of flux that are perpendicular to the coil's plane (Figure 2.5 - middle) which is usually placed tangential to the scalp (Hallett, 2007; Nollet, 2003). This placement corresponds with another electromagnetic principle that follows Maxwell's equations, by which the angle of the induced magnetic field will influence the induced electric current, with maximal current induction occurring when the conductive medium is perpendicular to the magnetic field. The third principle is that a changing magnetic field will induce an electrical current eddy (circulating) in a conductive medium, and is based on Faraday's law of induction. When applying TMS over the scalp, the neural tissue will serve as the conductor for electrical current conduction, rather than inducing currents in the scalp, skull, and meninges which are poor conductors (Nollet, 2003; Rothwell, 1997). These induced electrical currents in the neural tissue are parallel to the magnetic coil's plane (and perpendicular to the magnetic field) but flow in the opposite direction to the electric current flowing through the coil (clockwise-anticlockwise) (see Figure 2.5 - right) (Kapogiannis & Wassermann, 2008).

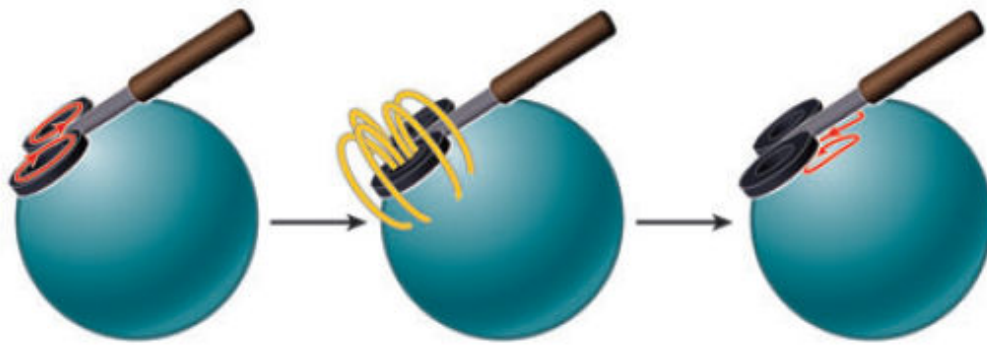


Figure 2.5 Left: electrical current in coil, middle: magnetic field with lines of flux, perpendicular to the coil's plane, right: induced electrical current in the conductor (from Wagner, Valero-Cabre, & Pascual-Leone, 2007).

In order for the magnetic field to be an effective stimulator, a short rise time (100-200 μ s) of the discharged electrical current (by the capacitor) and the discharged magnetic field (by the coil) are needed to induce a large circulating current sufficient to stimulate the neural tissue (Walsh & Pascual-Leone, 2003). A quick rise time is an important factor for stimulation of neurons. The electric current created in the neural tissue will stimulate the neurons and generate an action potential if it is large and quick enough to prevent the neurons from losing the electrical charge since neurons cannot accumulate the induced energy very well (Walsh & Pascual-Leone, 2003). The magnetic pulse can be either monophasic or biphasic.

For circular coils, the electrical field is highest at the coil's circumference. In addition, the bigger the coil's circumference, the deeper the penetration of the electrical field is (Wassermann et al., 2008). The figure-of-8 coil (see Figure 2.5) is composed of two small circular coils with current flowing in opposite directions that sums at the coil's junction and thus provide focal stimulation with maximal electrical field under the junction region between the two coils (L. G. Cohen et al., 1990; Rothwell, 1997). Thus, circular coils offer a more generalized and deeper stimulation of the neural substrate with less ability to define the site of stimulation, versus figure-of-8 coils that offer localized site of activation (Nollet, 2003) but with less penetration depth of the electrical field due to their relatively smaller individual coils. The strength of the magnetic field attenuates rapidly at deeper depths as a quadratic function of the distance from the coil, and the stimulated area decreases in size as a function of depth. The effective stimulation depth of a figure-of-8 coil is limited to ~1.5-2.1 cm of the cerebral cortex (Epstein, Schwartzberg, Davey, & Sudderth, 1990; Salvador, Silva, Basser, & Miranda, 2011; Zangen, Roth, Voller, & Hallett, 2005; Ziemann, 2003). The depth of penetration depends on the intensity of stimulation, with higher intensities stimulating deeper neural tissue and a larger area (Barker, 1999; Walsh & Pascual-Leone, 2003).

The size of the stimulated area depends on the depth of neural tissue below the coil. At a depth of 22 mm, the stimulated area is of ~4 x 3 cm. At a 15 mm depth, the stimulated area is ~4.5 x 5.5 cm (Barker, 1999; Walsh & Pascual-Leone, 2003). Hence, neurons within the cerebral cortex lying 1-2 cm from the scalp surface, and the central sulcus, which is 2 cm in depth, can be stimulated (Epstein et al., 1990; Nollet, 2003; Ziemann, 2003; Ziemann & Rothwell, 2000).

Two types of neuronal cells exist in the cortex: pyramidal cells, which account for 75% of all cortical neurons (Nolte, 2002), and non-pyramidal cells. The pyramidal cells are arranged in a perpendicular (upright) orientation to the cortical surface and most of them send axons that leave the cortex. The non-pyramidal cells (stellate cells) have axons in a different orientation, either perpendicular or tangential to the cortical surface (Standring, 2005). Hence, cortical nerve fibres are mostly perpendicular to the cortical surface but can also be tangentially oriented (Silva, Basser, & Miranda, 2008).

In order to stimulate the axon to produce neural activity, a difference in the induced electrical potential between 2 points along the neuron's membrane must exist. Briefly, neurons have a resting potential, which represents a state of imbalance in polarity and ion composition between the negative intra-cellular potential and the positive extra-cellular potential. The neuron is hyperpolarized (increase in cell negativity) at the point in which the current enters it, and depolarized (decrease its negativity, i.e., become more positive) at the point at which the current exits it. If the depolarization of the cell membrane is sufficient, the neuron's activation threshold is exceeded, causing a rapid inward flow of Na^+ ions into the cell through ionic channels in the cell membrane, and an action potential is generated.

A fast rate of change of the electric field will cause neural activation (Barker, 1999). In addition, TMS-induced activation of neurons also results from the spatial derivative of the electric field around the cell's membrane. If the induced electrical field is uniform along the membrane, no stimulation will occur. A difference in the electric field across the neuron will occur by the axon bending across the electrical field, or if the electrical field crosses a straight axon (see Figure 2.6 for more details). Thus, for a circular coil, if a hypothetical circular axon would have run parallel to the electrical field it could not be stimulated since the electrical potential along it would be equal. Stimulation will occur in axons that are bent out of this circle because the electrical field will be 'cut' and the axonal points near that bend will have different electrical potential and this will result in stimulation at that point (Rothwell, 1997). Similarly, for a figure-of-8 coil, a straight axon that runs underneath the junction region of the coil will not be depolarized (Rothwell, 1997).

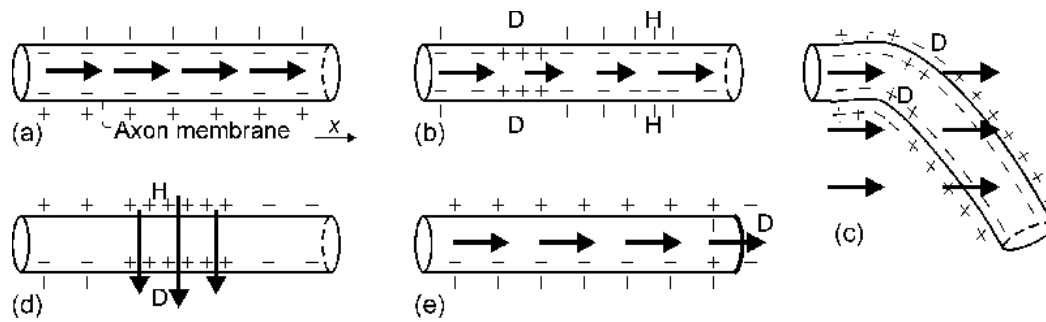


Figure 2.6 Activation mechanisms: (a) The electric field is parallel to the neuron course, thus no difference in the electric field will occur along the cell's membrane and, hence, no activation. (b) A non-uniform electric field along the axon will change the membrane's potential and causes gradient activation of the neuron. (c) The neuron bends in relation to the electric field which causes differences in the trans-membrane potential and, hence, activation. (d) The electric field crosses through a straight neuron, causing activation. (e) The axon terminal is depolarized (an effective field gradient can exist when an axon is abruptly terminated), causing activation. In addition, activation can occur where there is a change in the distribution of the electric field due to stimulation at the point at which a neuron emerges from a bony foramen. Also, axon terminations have lower thresholds and are more prone to depolarization than other sites of the axon (Maccabee, Amassian, Eberle, & Cracco, 1993). *D* represents depolarization, *H* represents hyperpolarization, black arrows represent electric field and current due to external stimulation (from Walsh & Pascual-Leone, 2003).

The figure-of-8 coil provides focal stimulation by inducing an electric field under its centre where its wings meet. An axon that runs horizontally to the coils' plane (perpendicular to the magnetic field) will be hyperpolarized by the 'virtual anode' created at the coils centre, close to its handle, and depolarized by the 'virtual cathode' created at the coil's centre away from the handle (Barker, 1999; Walsh & Pascual-Leone, 2003).

The orientation of cortical neurons in relation to the induced electrical current is influenced by the orientation of the neuron and by cortical folding (Salvador et al., 2011). Tangentially-induced currents are more likely to stimulate horizontal neurons that lie in the crown of the gyrus (Day et al., 1989) or the pyramidal neurons that lie in the walls of the sulcus (Fox et al., 2004). Based on a model of a simplified cortical sulcus that took into account cortical geometry and neurons orientation, the following sites may be stimulated. (1) terminations of medium-calibre horizontal fibres located at the crown of the gyrus and aligned with the induced current; (2) stimulation can occur at terminations of medium-calibre intracortical vertical axons; vertical pyramidal axon collaterals; and terminations of pyramidal afferents located near the lip of the gyrus; (3) stimulation can occur outside the cortex, where the gray and white matter meet, where sharp bends of pyramidal fibres with big diameter occur, just below the lip of the gyrus. Lastly, (4) stimulation can affect bend of Betz cells along the vertical wall of the sulcus (Silva et al., 2008).

Fibres with a larger diameter are more likely to be stimulated than smaller ones (Silva et al., 2008). Axons that are closer to the cortical surface, and thus to the coil, will be more easily stimulated, depending on their orientation. Parallel superficial axons will be more easily stimulated than parallel and deeper neurons. Neurons lying perpendicular to the coil's plane are more difficult to stimulate. Neurons that are not perfectly parallel to the coil will be stimulated as well but their distance from the coil will determine the ease of stimulation, with a closer location leading the more effective stimulation (Salvador et al., 2011).

The site of neural stimulation by the induced magnetic current is still under investigation. TES studies showed that since the dendrites have high resistance to an electric current, it is more likely that the current will enter the neuron at the cell body and exit at the first or second node of the axon (Amassian, Stewart, Quirk, & Rosenthal, 1987; Rothwell, 1997). However, since the ion channels of the axon respond to electric stimulation, they are considered to be more reactive to magnetically-induced currents, than the neuronal soma or dendrites (Mills, 1999; Salvador et al., 2011). TMS is more likely to stimulate neurons that have a parallel course to the cortical surface whereas TES can directly stimulate pyramidal neurons that are perpendicular to the cortical surface.

The motor evoked potential

TMS's capacity to measure neural excitability and changes in excitability is due to its ability to access and record synaptic response and synaptic plastic changes (Monfils, Plautz, & Kleim, 2005). To clarify, motor movements are represented by neuronal groups (Mountcastle, 1997) which are connected by dense horizontally-oriented neurons. Due to the magnetic pulse spread characteristics, when the coil is held above and tangential to the head, its current maximally activates these horizontal afferent intracortical neurons, rather than directly activating the pyramidal neurons due to their perpendicular orientation to the electric plane (Kapogiannis & Wassermann, 2008). Both excitatory and inhibitory interneurons that lie within the stimulated cortical area can be excited (Walsh & Pascual-Leone, 2003). The evoked motor response depends on the recruitment of the pyramidal tract neurons by afferent intracortical neurons via synaptic connections. Hence, changes in MEP characteristics, like magnitude and latency, will primarily reflect changes in intracortical connectivity (Monfils et al., 2005). An expansion of cortical maps can reflect creation of new synapses between neuronal groups, as a consequence of skill learning for example. But not only cortical maps can be evaluated with TMS. The evoked MEP can be assessed for changes in magnitude and latency. The assumption is that greater magnitude reflects strengthening of existing synapses of intracortical afferent or creation of new synapses (Kelly, Foxe, & Garavan, 2006). Shorter latencies are assumed to represent increased dexterity, based on

findings regarding decreased central motor conduction times in response to TMS that were linked to maturation and improvement in motor control (Fietzek et al., 2000).

MEPs are measured at the muscle level by either intramuscular or sEMG electrodes (Gooden et al., 1999) and represent the muscle activity induced by TMS stimulation of the primary motor area. Its magnitude is also dependent on the pre-stimulus activation level of the muscle (i.e., rest versus different contraction levels) and the stimulus intensity (Darling, Wolf, & Butler, 2006). In general, the magnitude of an MEP increases with an increased level of stimulation and with increased pre-stimulus muscle activation (Darling et al., 2006).

Descending volleys

The MEP response represents temporal and spatial summation of the descending volleys from the motor cortex to the brainstem (corticobulbar pathway) or to the spinal cord (corticospinal pathway). Either pathway will result in activation of alpha motor neurons that will, in turn, cause muscle contraction (Kapogiannis & Wassermann, 2008). The MEP response can be composed of early and late volleys. The initial and early waves are produced by direct excitation of pyramidal axons, either corticospinal for limb muscles or corticobulbar in the case of swallowing muscles, and are called D-(direct) waves. The later volleys represent indirect excitation of the pyramidal cells and are called I-(indirect) waves. A time delay of 1–2 ms accounts for the time taken for the neural signal to transmit from cortical interneurons to pyramidal neurons (Walsh & Pascual-Leone, 2003). This indirect excitation can be composed of either monosynaptic or polysynaptic connections (Ziemann & Rothwell, 2000), thus consisting of one or more interneurons (Amassian et al., 1987; Patton & Amassian, 1954). The variation in latency of I-waves (i.e., between 1-2 ms after D-waves) (Rosenthal, Waller, & Amassian, 1967) is an indicator of different sources of the descending volleys composing the I-waves, each sending excitatory signals at a slightly different time. The exact model for I-wave generation is not clear (Ziemann & Rothwell, 2000). It is important to emphasize that by recording an MEP to a single TMS stimulation, it is impossible to distinguish between I-waves and D-waves just by visually examining the MEP response (Ziemann et al., 1998). In addition, it is unclear which neural structures generate I-waves. The only structure that has been ruled out is the thalamus since lesions to it do not abolish I-waves, thus thalamocortical afferents are not involved in I-wave generation (Amassian et al., 1987).

In general, induced MEP responses are characterized by high between-trials variability of magnitude and shape, even in the presence of constant stimulus parameters (Kiers, Cros, Chiappa, & Fang, 1993). Induced activation of the corticospinal or corticobulbar pathway can represent both excitatory and inhibitory post-synaptic potentials (Cowan, Day, Marsden, & Rothwell,

1986). In addition, changes in the cortical levels of excitability will result in activating different number of motor neurons, which will affect MEP magnitude.

Factors influencing the MEP magnitude

Interpretation of MEP size is not straightforward since it is influenced by physiological mechanisms that are difficult to control for and difficult to predict, including (1) the number of motor neurons recruited, (2) the number of motor neurons with multiple discharge, and (3) synchronization of the motor unit discharge (Wassermann et al., 2008).

As mentioned, the excitability of the corticobulbar or the corticospinal pathway can also influence MEP size. Voluntary contraction facilitates the MEP response by shortening the latency and increasing the size of the MEP and also reducing the threshold for activation (Wassermann et al., 2008). Enhanced facilitation occurs when TMS is triggered at the peak of the EMG burst of the pre-activated muscle (Hinder, Schmidt, Garry, & Summers, 2010; Liepert, Dettmers, Terborg, & Weiller, 2001; Sohn, Jung, Kaelin-Lang, & Hallett, 2003). A higher number of discharging motor neurons results in increased excitability and an increase in MEP size, and voluntary contraction is likely related to increases in the amount of firing motor neurons (Wassermann et al., 2008). Conversely, muscle fatigue reduces MEP size (Taylor & Gandevia, 2001).

Repetitive motor neuron discharge can affect MEP size. Repetitive discharge is an indirect result of the succession of the descending volleys (D- and I-waves) from the cortex that converge upon the motor neurons, leading to repeated discharge (Amassian et al., 1987; Day et al., 1989; Patton & Amassian, 1954). This repetitive discharge may increase the size of the MEP and occurs with high intensity stimulation (Z'Graggen, Humm, Durisch, Magistis, & Rösler, 2005). In addition, an MEP size is relatively small due to desynchronization of the motor neuron discharge (Rösler et al., 2002). Desynchronization will result in phase cancellation, meaning that the positive phase of one motor unit will tend to be cancelled by the negative phase of another motor unit (Rösler, Roth, & Magistis, 2008) (See discussion below).

Increased intensity of magnetic stimulation results in increase MEP size. Saturation in MEP size occurs with stronger stimulation. At saturation level, the MEP does not reach a maximal magnitude and maintain it (i.e., reaches a plateau), but rather changes, in terms of small decrease or increase in magnitude, with an additional increase in the intensity of the magnetic (Wassermann et al., 2008).

Phase cancellation

MEPs are the product of the EMG signal recorded from the designated muscle(s) following TMS elicitation. Since the EMG waveform represents the simple summation of motor unit action potentials, they are susceptible to phase cancellation (Day & Hulliger, 2001). Motor unit action potentials contain positive and negative phases. Summation of those phases can result in an additive or constructive algebraic product or can result in a subtractive or destructive algebraic product (i.e., phase cancellation) (McGill, 2004). In a situation of synchronized isolated motor unit firing, phase cancellation will not occur in the recorded EMG signal. However, motor unit potentials are not monophasic but rather are bi- or tri-phasic with several active motor units firing. sEMG can thus underestimate the descending activation signals from the alpha motor neurons due to this cancellation (Day & Hulliger, 2001). A possible solution to phase cancellation might be to measure monophasic potentials rather than biphasic potentials, thus using a monophasic electrode (i.e., one recording electrode) rather than biphasic electrodes (i.e. two recording electrodes for that same muscle). However monopolar EMG is more prone to noise (Staudenmann, Roeleveld, Stegeman, & van Dieën, 2010). In a study that utilized controlled application of electrical stimulation to a designated number of alpha motor neuron axons, it was found that when the magnitude of the EMG signal was estimated as the sum of the rectified motor unit action potential trains, rather than the sum of the raw unrectified signal, a linear relationship was found between EMG magnitude and motor unit activation rate (Day & Hulliger, 2001). Hence, calculating the area of the MEP rather than its amplitude was proposed to be a better approach to estimate MEP magnitude because the area is less affected by this desynchronization (Rösler et al., 2002; Z'Graggen et al., 2005).

Stimulation localization

TMS has been found to be quite specific and focal when locating the hand area of the primary motor cortex. Studies that compared the activated area by TMS to concurrent fMRI (Sarfeld et al., 2012) and PET studies indicate good accuracy of TMS localization, with a 5-22 mm deviation from the PET activation foci (Wassermann et al., 1996). However, it is important to remember that TMS induces trans-synaptic activation that can indirectly activate other deeper or distant areas from the stimulation locus (Day et al., 1989; Walsh & Pascual-Leone, 2003). When providing magnetic stimulation over the motor cortex we can only claim that “we will be able to stimulate an unknown number of different kinds of neurons in the vicinity of the motor cortex” (Walsh & Pascual-Leone, 2003, p.55).

Swallowing-related MEPs

In swallowing research, TMS has been used as a neurophysiologic assessment tool to document magnitudes and latencies of MEPs during different swallowing tasks, such as water or saliva swallowing (Al-Toubi et al., 2011; Doeltgen, Ridding, Dalrymple-Alford, & Huckabee, 2011; Macrae, 2011), and following swallowing-related intervention (Abdul Wahab et al., 2010; Doeltgen et al., 2010; Macrae, 2011) in order to document the accompanied changes in neural excitability. TMS has also been used to document changes in swallowing related cortical maps associated with swallowing recovery following stroke (Fraser et al., 2002; Hamdy et al., 1996; Hamdy, Aziz, Rothwell, Crone, et al., 1997; Hamdy, Aziz, et al., 1998). Since TMS activates neurons that create synaptic connection with pyramidal cells (Rothwell, 1997), changes in the efficacy of the synaptic connection will be detected by measuring the magnitude of the MEP. It was suggested that decreased efficacy will result in decreased MEP magnitude and increased efficacy will result in increased MEP magnitude (Touge, Gerschlag, Brown, & Rothwell, 2001). Alternatively, decreased MEP magnitude might reflect cortical inhibition mechanisms (Peinemann, Lehner, Conrad, & Siebner, 2001). Therefore, changes to the neural level by either swallowing-related intervention or neural recovery will be registered as changes to the motor-evoked response to TMS.

MEPs have been recorded from the submental muscle group (Abdul Wahab et al., 2010; Al-Toubi et al., 2011; Doeltgen et al., 2010), pharynx (Fraser et al., 2002, 2003; Hamdy, Rothwell, et al., 1998) and oesophagus (Aziz et al., 1994; Fraser et al., 2003; Hamdy, Rothwell, et al., 1998). MEPs recordings can be obtained from individual motor units using needle EMG or from several motor units by sEMG (Day et al., 1989). Comparison of intramuscular EMG to sEMG recordings from right and left sides of anterior belly of digastric muscle revealed that sEMG recordings are influenced by cross-talk between the two sides, meaning that the activity of one digastric can be recorded from electrodes placed on either side. However, intramuscular recordings showed no cross-talk between recordings (Gooden et al., 1999). These results indicate that isolating the right and left electrical activation of the digastric muscle using sEMG is not possible. However, the collective response of the submental muscle group is of more interest due to its synergic role in swallowing. The submental muscles have been studied as a group in several projects focusing on swallowing biomechanics (Crary, Carnaby-Mann, & Groher, 2007; Steele & Huckabee, 2007; Wheeler-Hegland et al., 2008) and in studies of recorded MEP-induced responses (Abdul Wahab et al., 2010; Al-Toubi et al., 2011; Doeltgen et al., 2010, 2011)

Measuring the motor-evoked response following TMS allows an indirect measurement of long-term potentiation (LTP) and long-term depression (LTD) processes that take place at the cortical level and reflect synaptic connectivity of the intracortical interneurons. Support to the proposed

link between LTP occurrence and increased MEP magnitude and, vice versa, between LTD and decreased MEP magnitude emerges from repetitive transcranial magnetic stimulation (rTMS) studies. After application of excitatory rTMS (high frequency stimulation rate) the MEP response had increased amplitude (Maeda, Keenan, Tormos, Topka, & Pascual-Leone, 2000; Peinemann et al., 2004; Quartarone et al., 2005). However, after application of inhibitory rTMS (low frequency stimulation rate) the MEP amplitude decreased (Maeda et al., 2000; Touge et al., 2001). Applying rTMS can lead to changes in MEP that last up to 1 hour (Touge et al., 2001) but it has also been shown that LTP/LTD can take place for up to 2 hours after induction (Thompson, Mattison, & Nestor, 2005). Several swallowing studies documented MEP over a time period post-induction. Doeltgen et al. (2010) used TMS to document changes in corticobulbar excitability following application of different neuromuscular electrical stimulation (NMES) parameters, during swallowing and submental muscle contraction. MEPs from the submental muscle group were measured at several time points: immediately after intervention and at 30 min, 60 min, and 90 min post NMES. Increased MEP amplitude was found during a volitional contraction task at 30 min and 60 min post 80 Hz event-related NMES intervention. Swallowing MEPs were not affected by NMES and no changes in latency were found for either swallowing or contraction tasks (Doeltgen et al., 2010). The results of this study suggest that NMES can affect one activation network (for contraction) but not the other (for swallowing). A continuing study (Heck, Doeltgen, & Huckabee, 2012) measured the effects of the same NMES paradigm on the biomechanical level in order to allow for an insight into the possible association between neurophysiological and biomechanical changes. The pressure events in the pharynx and UES were measured before, during, and at 5 min, 30 min, and 60 min after NMES to the collective suprahyoid muscles in healthy young adults. A *reduction* in peak pressure at the level of the hypopharynx, but not at the oropharynx, was present at 5 min, 30 min, and 60 min post-stimulation during non-effortful saliva swallowing. Interestingly, Doeltgen et al. (2010) found an *increased* in excitability at 30 and 90 min post NMES. However, the increase in MEP magnitude was present only for volitional contraction of the submental muscles, and not for swallowing. In addition, following NMES, a reduction in UES pressure was measured at 5 min and 30 min post-stimulation (Heck et al., 2012). Thus, it is possible that NMES had different effects on swallowing and volitional contraction. Alternatively, it is possible that increased excitability translates to a reduction in the hypopharyngeal pressure, which is a possible negative outcome, and reduction in UES pressure, which is a positive outcome. Reduced UES pressure that is probably related to increased hyoid excursion, which is likely to be influenced from NMES application over suprahyoid muscles. Another study documented an increase in MEP amplitude during volitional swallowing at 30-, 60-, and 90-min post-presentation of a combined lemon smell and taste stimulus, but not after presentation of smell or taste stimuli separately (Abdul Wahab et al., 2010). MEPs recorded during volitional submental muscle contraction increased in amplitude only at 90 min post odour

stimulus in comparison to baseline. No changes in latency were documented in this study. The results of these two TMS studies (Abdul Wahab et al., 2010; Doeltgen et al., 2010) suggest that different types of intervention might affect different neural control networks. In addition, MEP magnitude appears to be more sensitive outcome measure than latency, which seems to be a relatively stable outcome measure for swallowing MEPs before and after intervention. Other studies measured changes in MEP over time following rTMS (Fraser et al., 2002), water swallowing, pharyngeal stimulation, and oropharyngeal anaesthesia (Fraser et al., 2003), and following painful and non-painful oesophageal distension (Hamdy et al., 2002) with different effects of those tasks on MEPs.

In order to differentiate between the effects of swallowing-related intervention and the effects of repetition of the motor act of swallowing on MEPs, Al-Toubi et al. (2011) documented MEP magnitudes and latencies over a 2-hour period following 60 repetitions of volitional saliva swallowing and following a control task that involved 25 min rest. MEPs were collected from the submental muscle group with midline electrode position during 2 tasks: voluntary muscle contraction of the submental muscles and volitional saliva swallowing. MEPs were collected for both tasks at baseline and after the rest or after the 60 swallows at 4 time points: 5, 30, 60 and 90 min. The results indicate that MEP magnitudes and latencies do not change over time just as a result of repeated measures (Al-Toubi et al., 2011; Doeltgen, Ridding, O'Beirne, Dalrymple-Alford, & Huckabee, 2009) and also that they do not change following consecutive saliva swallowing (Al-Toubi et al., 2011). However, the variance was quite large, with a standard deviation of approximately 35-55% of the mean in one study (Doeltgen, Ridding, et al., 2009) and reaching up to approximately 75% in another study (Al-Toubi et al., 2011). These results, paired with intervention studies reporting increased MEP magnitudes (Abdul Wahab et al., 2010; Doeltgen et al., 2010), indicate that in order to affect corticobulbar excitability, simply repeating swallowing is not enough. However, specific intervention, for example MNES and smell and taste, can change excitability and this change can be measured from the submental muscle group at midline position (Abdul Wahab et al., 2010; Doeltgen et al., 2010). Thus, it is possible to detect cortical excitability changes during volitional swallowing and submental contraction by recording MEPs from the submental muscle group. Links between biomechanical and neurophysiological changes following NMES intervention have been indirectly assessed (Doeltgen et al., 2010; Heck et al., 2012). However, data were not collected at the same time with the same subjects, but rather in two different studies, with Doeltgen et al., (2010) measuring MEPs, and Heck et al., (2012) measuring pharyngeal pressure, following an identical NMES protocol. Hence, the nature of the increase in MEP magnitude is still not clear; increased magnitude can be related to positive and enhancing effects or negative and risk-posing effects on swallowing function.

Genetic factors can influence the capacity for plastic changes following behavioural intervention. TMS induced responses can capture those changes. Individuals carrying val66met polymorphism of the brain-derived neurotrophic factor (BDNF) exhibited reduced MEP changes in response to motor training in comparison to individuals without this polymorphism (Kleim et al., 2006). Thus, behaviourally-driven increases in neural activity are influenced by genetic factors which can be manifested in post training MEPs. This can potentially influence swallowing-related intervention results, but is yet to be explored.

In the swallowing studies mentioned above, MEPs could not have been elicited in the entire group of subjects recruited. In one study, 50% (8 out of 16) had swallowing MEP, and 100% had contraction-related MEP (Abdul Wahab et al., 2010). In another study (Doeltgen et al., 2010), 28% (4 out of 14) and 21% (4 out of 19) did not have contraction-related MEPs. In another study from the same group, 38% of the subjects (13 of 35) had neither swallowing- nor contraction-related MEPs. Of the 22 who had measurable contraction-related MEPs, 6 (27% of 22) did not have recordable swallowing-related MEPs. This lack of ability to record either swallowing related or contraction related MEPs from all subjects was hypothesized to be a result of the TMS coil position and its angle over the scalp which influenced its ability of the induced effective electromagnetic field to stimulate the neurons of interest (Doeltgen et al., 2010). In addition, the distance between the coil and the motor cortex changes the ability to elicit strong enough stimulation; the distance might be influenced by skull thickness or cerebral atrophy (Wassermann et al., 2008) which is known to occur with increased age (Gur et al., 1991). In addition, differences in swallowing-related MEPs and contraction-related MEPs are thought to be related to a relatively small number of horizontal afferent neurons from S1 to M1 that participate in swallowing execution, versus a larger number of horizontal afferents that participate in contraction which is a more cortically-driven motor activity. Another explanation is related to the low signal-to-noise ratio of swallowing-related MEPs (Doeltgen et al., 2011). The small magnitude of swallowing MEPs might be due to a relatively small contribution of M1 to swallowing execution.

When using a figure-of-8 coil, its orientation is important since it affects the spread of the electrical current. This was considered as an alternative explanation to the variability found in test-retest swallowing-related MEP (Plowman, Triggs, Malcolm, & Rosenbek, 2008). Different orientations have been reported in swallowing research. Many research studies (Abdul Wahab et al., 2010; Al-Toubi et al., 2011; Gooden et al., 1999; Gow, Rothwell, Hobson, Thompson, & Hamdy, 2004; Macrae, 2011) have used a 45-deg angle to the midsagittal (midsagittal plane of the head– line between nasion and inion) plane with the coil handle positioned posteriorly. A zero-deg angle position to the coronal plane (ear to ear line) with posteriorly-oriented coil handle (i.e., perpendicular to the central sulcus) has been used as well (Plowman et al., 2008). Some studies

did not specify the coil's orientation (Fraser et al., 2003; Sowman et al., 2009). I-waves are elicited when the magnetic current runs from posterior to anterior direction when the coil is held perpendicular to the central sulcus (sagittal plan). However, when the current is directed lateral to medial, and the coil is held parallel with the central sulcus, D-waves are elicited (Ziemann & Rothwell, 2000).

2.4.2 Measuring the submental muscles and hyoid movement

Hyoid excursion during the pharyngeal stage of swallowing has an important role in protecting the airway from aspiration of the ingested bolus by contributing to epiglottic deflection and also to UES opening to allow bolus transfer. Hyoid excursion is achieved primarily by submental muscle group contraction, which includes the anterior belly of the digastric, geniohyoid, and mylohyoid muscles (Daniels & Huckabee, 2008; Dodds et al., 1989; Dodds, Logemann, & Stewart, 1990; Doty & Bosma, 1956). Studies have documented a correlation between submental muscle activity and hyoid excursion, and reported on the close temporal relationship between the peak of the submental EMG waveform and the peak of anterior hyoid movement (Cook et al., 1989; Crary, Carnaby-Mann, & Groher, 2006; Perlman, Palmer, McCulloch, & Vandaele, 1999a; Shaker et al., 1990). Alterations in hyoid movement as a consequence of dysphagia were found to coincide with alterations in submental muscle activity (Lazarus et al., 1996; Martino et al., 2001). Investigation of submental muscle activity and hyoid movement has been of interest in swallowing research and more specifically in regards to dysphagia rehabilitation. Thus, assessing the effects of swallowing training on the submental muscles and hyoid movement is an important outcome measure.

There are some reports in the literature regarding the effects of swallowing-training on submental muscle size and activation, and on hyoid movement. Execution of behavioural swallowing manoeuvres, including effortful swallowing, were shown to cause immediate effects on both hyoid movement and submental activation (Bülow, Olsson, & Ekberg, 1999; Hind, Nicosia, Roecker, Carnes, & Robbins, 2001; Huckabee & Steele, 2006; Wheeler-Hegland et al., 2008). Studies of the cumulative effects of swallowing exercise on hyoid movement have found both changes (Logemann et al., 2009) and no changes (Macrae, 2011; Shaker et al., 1997). Changes to the size and activity of submental muscles have also been investigated but with no measurable effects identified (Macrae, 2011).

It has been reported that swallowing performances on repeated swallowing trials at a given time point can have considerable variability from one trial to the other, with some subjects showing more variability than others (Lof & Robbins, 1990). Swallowing is a highly adaptive motor

activity and, thus, high levels of variability in swallowing function are expected with different boli and different subjects (Gay, Rendell, Spiro, Mosier, & Lurie, 1994). Thus, when measuring swallowing biomechanics, assessing a single swallow may not represent the actual capability of the subject and several swallowing trials should be included (Lof & Robbins, 1990).

The next sections include a discussion on measurement of hyoid movement and submental muscle area using ultrasonography, and measurement of submental muscle activity using sEMG.

2.4.2.1 *Measuring hyoid movement using ultrasonography*

Ultrasonography biophysics

Ultrasound is a safe, low cost, and widely used assessment tool. The ultrasound transducer converts electrical energy into sound waves that are transmitted into the body's tissues, and then measure returning echoes by converting them from sounds-waves into electrical energy. Their return latency is an indicator of the depth of the structure (or its reflection point) relative to the transducer: a later return indicates a deeper structure and an early return indicates superficial structures (Walker, 2004). Body tissues have different densities, thus the sound wave propagates through them at different velocities. This determines the strength of the reflection: non-dense tissues, like air, water, and fat, allow fast travel of the sound wave and appear as hyperechoic and bright. In addition, non-dense tissues have low acoustic impedance, meaning that their molecules have low resistance to sound transmission. Dense tissues like muscles and bones and hypertrophic muscles result in a slower sound travel speed and appear dark or hypoechoic and have high acoustic impedance (Walker, 2004). Low impedance materials (like water) will allow the sound to travel deep and thus to image structures position behind them. High impedance materials (like bones) will create a barrier for the sound and will not allow visualization of deeper structures located behind them (Heggie, Liddell, & Maher, 2001).

Where tissues of different densities meet, they create an acoustic boundary for the sound wave. At this meeting point, part of the sound wave is reflected back and some is transmitted. The difference in density between the two tissues on either side of the interface will determine the amount of reflected sound. For example, muscle/air interface is a good sound reflector meaning that a large portion of the sound energy will be reflected back and a small portion will travel deeper, whereas muscle/fat has low reflection ratio, meaning that a large portion of the sound will travel deeper and small part will be reflected back (Shawker, Sonies, & Stone, 1984). The transducer detects reflected sound when it is perpendicular to the structure and the boundaries are best visualized in this position (Walker, 2004). Diffuse reflection of the sound wave is a result of a boundary that is not smooth, like most boundaries in the body (Heggie et al., 2001). When

sound waves travel through a medium, they lose energy, thus reflection from a superficial acoustic boundary will contain more energy than a reflection from a similar acoustic boundary at a greater depth.

The frequency of the sound wave also influences its depth of penetration: high frequency ultrasound allows clear visualization of superficial structures whereas low frequency ultrasound can penetrate deeper and allow clearer visualization of deeper structures (Walker, 2004). However, image clarity changes in relation to several factors, among which are the presence of fatty tissue, since resolution decreases with depth, subcutaneous fat tissue can influence imaging of muscles that lie underneath it.

The properties of the muscle can affect echoic levels: hypertrophic muscles will have hypoechoic appearance and, hence will appear darker. Hyperechoic appearance will be a consequence of reduction in muscle fibres and the muscle will appear brighter. (Walker, 2004). In addition to muscle appearance, contraction of the muscle will cause thickening, which also influences its cross sectional area (CSA). Thus, when imaging a contracted muscle versus non-contracted muscle, differences in the CSA will appear. However, not only temporary contraction can change the muscle's size - increased blood flow to the muscle as a consequence of motor exercise can increase muscle size by 10-15% (Walker, 2004). Thus, when performing repeated measures to quantify changes in the CSA following intervention, it is important to control for those possible confounding variables.

Stabilization of the head during measurement of oropharyngeal muscles

Since different positions can affect muscle contraction or relaxation level, stabilization is important for repeated measurements of muscle size within the same subject. Thus, measurement of size of muscles involved in swallowing is susceptible to confounds if stabilization is not controlled for. Muscles like the tongue and suprahyoid muscles are highly mobile and hard to stabilize, as opposed to limb muscles that have fixed insertion and origin points. In order to address these positioning issues, studies have employed various stabilization techniques, including that of head position and of transducer position in relation to the head (Chi-Fishman, 2005). Different stabilization devices have been described in the past, including the head and transducer support system (HATS) (Stone & Davis, 1995) and the cushioning scanning technique (CST) (Peng, Jost-Brinkmann, & Miethke, 1996), originally developed for imaging tongue movement. However, none of these systems has been found to be free of flaws. Controlling head/transducer position while using the HATS was not adequate and 'accidental' displacement occurred during data acquisition (Hueber et al., 2010). The CST was reported to be susceptible to movement artefact and impeded swallowing (Söder & Miller, 2002). These authors concluded

that a hand-held approach is more convenient for the subjects and transducer stabilization was easy to maintain. However, a hand-held approach may not be sufficient for a repeated-measures studies, since variance unrelated to the investigated process might be introduced. Macrae (2011) used a unit that stabilized the mouth in reference to the transducer. The angle and distance between the mouth and the submentally placed transducer, were controlled.

Assessing hyoid movement by ultrasonography

Hyoid movement has been assessed by VFSS (Gay et al., 1994; Leonard & McKenzie, 2006; Terk, Leder, & Burrell, 2007; Wheeler-Hegland et al., 2008), which is considered the ‘gold standard’ for assessing swallowing function during different swallowing tasks and swallowing manoeuvres (Rugiu, 2007). VFSS allows (i) identification and assessment of the swallowing structures, (ii) quantitative measurements of displacement events like laryngeal excursion and hyoid displacement, (iii) temporal measurements of parameters like onset of the pharyngeal swallowing and the duration of bolus passage through the pharynx, and (iv) identification of penetration and aspiration of the ingested bolus (Kendall, McKenzie, Leonard, Gonçalves, & Walker, 2000; Leonard, Kendall, McKenzie, Gonçalves, & Walker, 2000; Rugiu, 2007). VFSS has been used to assess swallowing difficulties (Dodds, Logemann, et al., 1990; Kang, Kim, Seo, & Seo, 2011; Nagaya, Kachi, Yamada, & Sumi, 2004; Power et al., 2007) and also to describe swallowing biomechanics among healthy subjects (Allen, White, Leonard, & Belafsky, 2010; Aminpour, Leonard, Fuller, & Belafsky, 2011; Cook et al., 1989; Kendall et al., 2000; Palmer et al., 1988). More specifically, hyolaryngeal excursion has been given attention in many studies and this important event has been quantified using VFSS among dysphagic patients (Power et al., 2007; Wang, Chang, Chen, Lin, & Hsiao, 2010) and healthy subjects (Leonard & McKenzie, 2006; Nakane, Tohara, Ouchi, Goto, & Uematsu, 2006; Wheeler-Hegland et al., 2008).

Measuring the cumulative effects of swallowing-related exercise on hyoid displacement has been conducted in the past with VFSS following the head-lift exercise (Shaker et al., 1997; Shaker, Easterling, et al., 2002), the tongue-strengthening exercise using the Iowa oral performance instrument (IOPI) (Robbins et al., 2005, 2007), and following the EMST exercise (Troche et al., 2010). The effects of head-lifts and tongue-strengthening exercises were first assessed using healthy subjects and then using dysphagic subjects by utilizing VFSS. The effects of EMST were first assessed using healthy subjects, however VFSS was not employed as a method of investigation in this population (Baker, Davenport, & Sapienza, 2005; Kim, Davenport, & Sapienza, 2009). Since VFSS exposes subjects to ionizing radiation, its use among healthy subjects should involve mindful consideration and be well supported from an ethical point of view. In regards to head-lift and tongue-strengthening exercises, earlier ground work was

conducted to estimate other biomechanical effects before exposing subjects to radiation (Nicosia et al., 2000; Ren et al., 1993; Robbins et al., 1995; Shaker et al., 1993).

Quantifying hyoid displacement is also possible through the use of ultrasonography. Several studies measured hyoid displacement with ultrasound among healthy and dysphagic patients (Chi-Fishman & Sonies, 2002a, 2002b; Kuhl, Eicke, Dieterich, & Urban, 2003; Macrae, 2011; Macrae, Doeltgen, Jones, & Huckabee, 2012; Scarborough, Waizenhofer, Siekemeyer, & Hughes, 2010; Sonies, Wang, & Sapper, 1996; Yabunaka et al., 2011). The hyoid bone cannot be directly viewed by ultrasonography since bones are hypoechoic and can only be visualized by the larger shadow they create (Walker, 2004). However, hyoid bone motion can be deduced by analyzing its acoustic shadow and the proximate muscle tissue (Sonies et al., 1996).

Hyoid displacement can be measured by calculating the difference between the position of the hyoid at rest and the position of the hyoid in maximum displacement when using VFSS for image acquisition (Leonard et al., 2000). Similarly, when using ultrasound, maximum hyoid displacement has been quantified by measuring the hyoid trajectory in relation to its rest position, so distances were calculated between the rest position and the point of maximum anterior displacement and beginning of the return to rest position (Yabunaka et al., 2011). Good within-session inter- and intra-rater reliabilities were found for quantifying hyoid displacement during saliva swallowing by using the mental spine of the mandible as a reference point to the hyoid. The distances between these two points at rest and at maximum displacement were calculated, and expressed as a percentage of change from rest to maximum displacement (Macrae et al., 2012).

Some studies indicate that ultrasonography measurement of hyoid displacement has the capacity to capture changes in this variable. Existing research indicates a reduction in maximum hyoid excursion with age among healthy participants (Yabunaka et al., 2011). In addition, the influence of medication on swallowing duration among patients with progressive supranuclear palsy was indicated by counting the number of frames from initial antero-superior hyoid movement to rest position of the video-loop recorded (Frattali, Sonies, Chi-Fishman, & Litvan, 1999). So far, ultrasound has been used as a tool to measure changes in hyoid displacement following swallowing-related exercise only once (Macrae, 2011).

2.4.2.2 *Measuring submental muscles size using ultrasonography*

Ultrasound has been documented to be a reliable and sensitive measurement tool for muscle size assessment (Brockmann et al., 2007; Emshoff, Bertram, & Strobl, 1999). It can be used to distinguish between pathologic and healthy muscle (of the leg) by measuring the muscle width but not its CSA. In addition, the same study found a moderately strong correlation between muscle

strength, measured during maximum isometric contraction, and muscle size measured by its width during contraction, with bigger muscles producing more strength. Interestingly, the relationship between the CSA and muscle force showed minimal correlation when measuring leg muscles (Chi-Fishman, Hicks, Cintas, Sonies, & Gerber, 2004). This might be due to complex relationship between the muscle length and thickness, tendon length, and fibre composition that contribute to muscle strength and force during maximum volitional contraction (Chi-Fishman et al., 2004).

Specific to the swallowing muscles, changes in muscle size can be detected by ultrasound and MRI. Robbins et al. (2005, 2007) demonstrated changes in tongue volume as measured by MRI following tongue-strengthening training. The CSA of some of the muscles involved in swallowing, including the submental muscle group (Emshoff et al., 1999; Shawker et al., 1984; Watkin et al., 2001), has been measured using ultrasound. The submental approach (Emshoff et al., 1999; Shawker et al., 1984; Watkin et al., 2001) visualizes the anterior belly of digastric, mylohyoid, geniohyoid and genioglossus. The anterior belly of digastric consist of two straight muscle bellies connected by a round intermediate tendon (Emshoff et al., 1999) and appears as two oval structures located on right on left sides on the midsagittal plane at a superficial location (Emshoff et al., 1999). The mylohyoid lies deeper and appears as a thin U shaped hypoechoic muscle (Jain, 2008). Deeper still lies the geniohyoid which is a paired muscle but, since its two bellies lie in close proximity, it appears as one hypoechoic structure (Jain, 2008) (Figure 2.7).

Measuring the CSA of the geniohyoid allowed for detection of differences in geniohyoid size between healthy young and old muscles and between healthy and pathologic muscles (Watkin et al., 2001). The geniohyoid muscles were measured using a 6-10 MHz linear transducer in a coronal plane in real-time B mode during rest and consonant pronunciation in young ($M = 27$ y) and old ($M = 69$ y) participants and in patients ($M = 62$ y) who received radiation following oral pharyngeal cancer. The geniohyoid was larger in the older group ($1.97 \pm 0.16 \text{ cm}^2$) and patient group ($2.44 \pm 0.18 \text{ cm}^2$) than the younger participants ($1.56 \pm 0.07 \text{ cm}^2$) (Watkin et al., 2001). This finding of increased CSA was consistent with other reports regarding increased fat and connective tissue in muscles with increased age (Heeneman & Brown, 1986) and increase in collagen and fibrotic tissue after radiotherapy (Remy, Wegrowski, Crechet, Martin, & Daburon, 1991; Yarnold & Brotons, 2010). Calculations were made for the midpoint of the muscle by counting the number of frames taken along the muscle length (Watkin et al., 2001).

The anterior belly of digastric muscles were measured in 46 patients with temporomandibular joint disorders using a linear B-scan 7.5 MHz transducer in a coronal (Emshoff et al., 1999). The anterior belly of digastric was not measurable in 4.3% of the images taken of the left and the right sides. However, for masseter and temporalis the failure rate in image acquisition was higher for

the left than right side, probably due to positioning of the examiner on the right side of the subject and difficulties with transducer orientation on the left side of the subject (Emshoff et al., 1999).

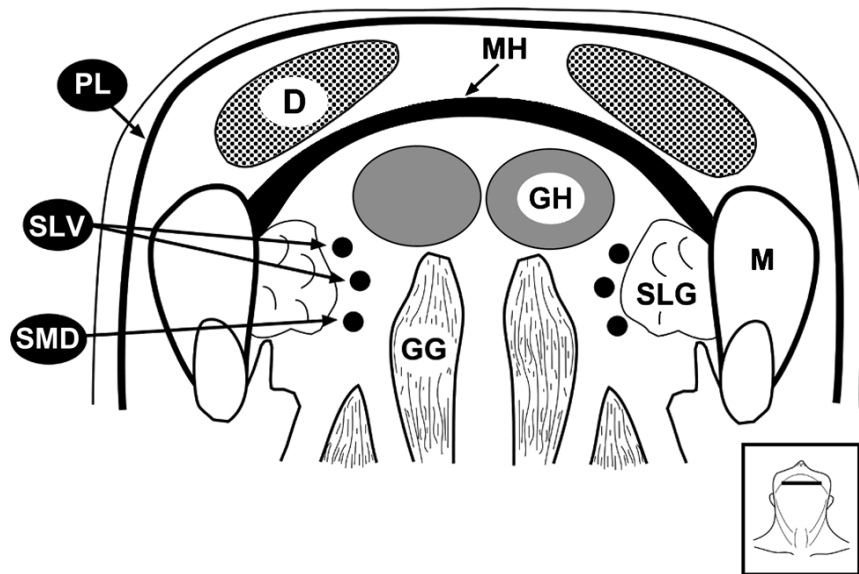


Figure 2.7 Submental region, coronal plane. Top: superficial structure. Bottom: deeper structures. D, anterior belly of the digastric; GG, genioglossus; GH, geniohyoid; M, mandible; MH, mylohyoid; SLG, sublingual gland; SMG, submandibular gland; SMD, submandibular duct; SLV, sublingual vessels; PL, platysma [from Jain, 2008].

One report documents the use ultrasonography to measure changes in the size of the submental muscles following training (Macrae, 2011). As mentioned before, it is important to account for positioning and stabilization of the muscles especially when measuring training effects outcomes in a repeated-measures study, such as that of Macrae (2011).

2.4.2.3 *Measuring submental muscle activity using sEMG*

Measuring EMG is an important outcome assessment in biomechanics studies since it provides an estimate of muscle force (Staudenmann et al., 2010) by measuring its activity (Palmer, Luschei, Jaffe, & McCulloch, 1999). There are two main methods to record EMG: intramuscular and surface electrodes. Intramuscular EMG electrodes are inserted into the muscle and are therefore an invasive measure of the activity of an individual muscle, and more precisely, a measure of the activity of a specific part of the muscle. Since the intramuscular electrodes have a small measuring space, its recording, or pick-up area is very restricted. sEMG records the global muscle activity in a non-invasive fashion (Hogrel, 2003). It allows measurement of the combined activity of a number of muscles that lie underneath the electrode (Palmer et al., 1999). This compound action potential is recorded from several motor units. This type of measurement method is

relevant when one wants to evaluate the function of a muscle or muscles in its proximity as a whole. Since the submental muscles (anterior belly of digastric, mylohyoid and geniohyoid), jointly activate in a synergistic pattern to pull the hyoid bone forward and upward during swallowing, measuring their activity as a group seems appropriate (Palmer et al., 1999; Wheeler-Hegland et al., 2008). Thus, this section focuses on the use of sEMG.

Biophysics of sEMG

Following cleaning of the skin area overlying the muscle of interest in order to remove dirt and oil, a pair of electrodes is attached to the skin in a bipolar configuration. A ground electrode is placed in a different location, in proximity to the recording electrodes. The EMG signal recorded from the two recording electrodes is amplified using a *differential amplifier*, which amplifies the difference between the electric signals at the two electrodes. Signals that are common to both electrodes are subtracted from each other and, hence, removed and are usually referred to as noise or artefacts (Tassinari & Cacioppo, 2000).

Briefly, muscles fibres are composed of fibrils bound by filaments that are made of proteins. Amongst them are actin and myosin. The filaments can change their length and this is manifested as a muscle twitch or contraction.

Following depolarization of the alpha motor neuron and transmission of action potential along the neuron's axon, neurotransmitters (mainly acetylcholine) are released into the neuromuscular junction, called *the motor end-plate*. The neurotransmitters cause depolarization of the resting potential of the muscle's cell membrane and a muscle action potential travels along the surface of the fibre and into the muscle, which results in muscle contraction. The contraction involves an ionic interaction between the proteins composing the filaments (actin and myosin). The changing electrical field associated with this process passes to the extra-cellular fluids and to the skin. Surface EMG electrodes placed on the skin record the voltage fluctuations arising from several muscle fibres within a motor unit, thus creating a motor-unit action potential. Generally, the activity is recorded from several motor units that lie underneath the electrodes. Thus, sEMG measures the electrical activity associated with those events and records the summated electrical potential of the muscles in its vicinity (Staudenmann et al., 2010; Tassinari & Cacioppo, 2000).

The relationship between EMG and muscle force

The relationship between EMG and force depends on the recruitment range of the motor unit and hence on the composition of muscle's fibre type (Staudenmann et al., 2010). A linear relationship between EMG and force was documented for muscles with a uniform fibre composition, whereas

a non-linear relationship was found for muscles with mixed fibre composition (Woods & Bigland-Ritchie, 1983).

An increase in the number of the activated motor units and greater discharge frequency results in an increased force. High force contraction will lead to an increase in the EMG amplitude which indirectly reflects increased recruitment of motor units and increase synchronization of the firing rate (Shinohara & Sogaard, 2006). In contrast, there are conflicting results regarding EMG amplitude of low-force fatiguing contractions. Reports of increase, decrease, or no change in EMG exist (Shinohara & Sogaard, 2006). Neuromuscular fatigue (reduction in force capacity) decreases the maximal force generation capacity as a result of a reduction in the discharge rates of the motor units. The reduction in the motor unit firing rate can be thought of as a way to maintain a constant force in the presence of reduced resources (fatigue). The decrease in discharge rate and the desynchronization of motor unit activation, due to grouping of fibres from different motor units, leads to phase cancellation of the electrical signal and thus a decrease in the EMG amplitude (Shinohara & Sogaard, 2006; Staudenmann et al., 2010).

Contradictory results have arisen from studies that utilized sEMG recordings in limb muscles. Motor unit action potentials recorded by sEMG from the quadriceps femoris muscle were found to have no correlation with isometric strength, endurance measurements, or work capacity, in healthy subjects and in subjects with pathological muscle findings (post-polio). In addition, the EMG recordings from both populations were not significantly different (Rodriguez & Agre, 1991). In contrast, EMG recordings from Huntington's disease patients indicated that sEMG can be used to quantify motor abnormalities (Walker, 2007), possibly due the nature of the motor disorder in Huntington's disease, which is characterized by chorea and changes in muscle activation patterns rather than weakness as in polio.

Recordings of muscles involved in swallowing demonstrated a positive, medium-sized correlation between force and the peak amplitude of the sEMG signals from masseter and temporal muscles recorded during a jaw opening task, although a higher correlation was detected when the EMG area was used for correlation with force (Ottenhoff, van der Bilt, van der Glas, Bosman, & Abbink, 1996).

sEMG recordings from the submental muscles

sEMG recordings from the submental muscle group have been used in many studies (Crary & Baldwin, 1997; Crary et al., 2006; Ertekin et al., 1997; Huckabee, Butler, Barclay, & Jit, 2005; Huckabee & Steele, 2006; Macrae, 2011; Perlman, Palmer, McCulloch, & Vandaele, 1999b; Shaker et al., 1990; Steele & Huckabee, 2007; Vaiman, Eviatar, & Segal, 2004). sEMG

measurements have been found to have the capacity to detect changes in the muscle activity during execution of swallowing manoeuvres and as a result of different bolus types. Changes in sEMG waveforms recorded during execution of swallowing manoeuvres were documented using sEMG, including effortful swallow (Huckabee & Steele, 2006; Wheeler-Hegland et al., 2008), Mendelsohn's manoeuvre (Wheeler-Hegland et al., 2008), head lifts (Yoshida, Groher, Crary, Mann, & Akagawa, 2007) and EMST (Wheeler-Hegland, Chiara, & Sapienza, 2007; Wheeler-Hegland et al., 2008). Bolus volume affected sEMG amplitude, with an increase in the volume of a liquid bolus (from 3 to 10 to 20 mL) resulting in increase in EMG amplitude (Ertekin et al., 1997). Saliva swallowing had higher sEMG amplitude than water boluses of 3-20 mL volume (Ertekin et al., 1997), presumably due to increased muscular effort needed to perform successive saliva swallows.

A correlation between submental activity and other biomechanical events has been explored. Several studies have explored the relationship between submental activation and the pharyngeal phase of swallowing. More specifically, a moderate-strong, positive correlation was found between the value of the maximum peak of the sEMG waveform and the degree of maximum hyoid excursion as measured with VFSS (Wheeler-Hegland et al., 2008). In addition, a strong positive correlation was found between the timing of the peak of the sEMG waveform and the timing of maximum hyoid displacement during normal swallowing and effortful swallowing, but not during execution of Mendelsohn manoeuvre and EMST (Wheeler-Hegland et al., 2008). Another study documented a relationship between the timing of the peak amplitude from the submental group and peak of hyolaryngeal elevation using ultrasound (Sonies, Gottlieb, Solomon, Matthews, & Huckabee, 1997). In addition to the relationship between submental activation and hyolaryngeal elevation, a relationship has also been found between submental activity and UES opening (Crary et al., 2006). Thus, submental muscles activation is closely related to the pharyngeal stage of swallowing, most likely due to the role of this muscle group in hyolaryngeal elevation which is one of the first events of pharyngeal swallowing (Ertekin et al., 1995).

However, inference from the sEMG signal to biomechanical events cannot always be made (Wheeler-Hegland et al., 2008). Contribution of the tongue muscles to the sEMG signal of the submental group has been explored in several papers. Huckabee and Steele (2006) reported that performing the effortful swallow with and without emphasis of tongue to palate contact influenced EMG recording from the submental area with increased peak amplitude associated with tongue to palate pressure. Their conclusion was that sEMG from the submental area is a non-specific measure of the floor of mouth muscle group and the recording might involve intrinsic tongue activation as well. However, co-occurrence of events does not necessarily indicate causality. In a another study, a correlational approach was taken, and the results showed that

tongue to palate pressure was not correlated to sEMG signals from the submental area during isometric and isotonic tasks (Lenius, Carnaby-Mann, & Crary, 2009). Another study ruled out the contribution of genioglossus, which is a relatively large muscle of the tongue, to the submental sEMG signal recorded during swallowing utilizing intramuscular electrodes and surface electrodes by showing low correlation value (Palmer et al., 1999). Thus, it seems that submental sEMG signal is associated with oral stage events like tongue pressure against the palate but there is no causal or correlational relationship. Increased tongue pressure might be accompanied by increased submental activation due to synergic activation of the two muscles group: tongue and floor-of-mouth. Only one study has measured sEMG from the submental area for assessing the cumulative effects of swallowing training, but no measurable effects were identified (Macrae, 2011).

2.4.3 Changes in pharyngeal pressure

Pharyngeal manometry has been used to measure the pharyngeal pressure events by quantifying the amplitude and duration of the pressure and also quantifying coordination or timing of those events by calculating the relative duration between pressure events registered by different sensors (Butler et al., 2009).

The manometry catheter is positioned through the nose. Correct location can be made by visual inspection of its location via mano-fluoroscopy or by the characteristic M-wave in case of 'blind' localization procedure using the pull-through technique (Butler et al., 2009; Huckabee et al., 2005; Olsson, Nilsson, & Ekberg, 1995). The M-wave is an M-shaped configuration that appears in the manometric waveform of the distal sensor during swallowing and signifies the location of that sensor in the top part of the UES (Olsson, Nilsson, et al., 1995). The first increase in the amplitude (the first spike of the M) represents the upward elevation of the tonically contracted UES toward the sensor. The subsequent pressure drop represents relaxation of the UES and thus its opening. The second rise in pressure represents closure of the UES and return to its tonic contraction. The final drop in pressure from the second peak to lower pressure represents the descent of the UES (Olsson, Nilsson, et al., 1995). Usually the distal sensor of the catheter is located at the level of the UES and, thus, the other sensors lie above it. The positioning of the lower sensor at the top part of the UES is important since during swallowing the larynx elevates and slides on the catheter. Positioning the catheter in the mid-zone or distal part of the UES might accidentally record the oesophageal wave during swallowing (Olsson, Nilsson, et al., 1995).

Manometry placement is usually well tolerated as documented in previous research that used a 2.1 mm wide catheter trans-nasally (Huckabee et al., 2005; Macrae, 2011; Witte, Huckabee,

Doeltgen, Gumbley, & Robb, 2008). Conversely, one study reported that 5 out of 20 healthy subjects could not tolerate a 3 mm diameter intraluminal catheter that was passed transorally (Plowman et al., 2008). Once inserted, the presence of the manometer did not change the temporal swallowing events (Cook et al., 1989).

Pharyngeal manometry can measure both contact pressure, which is the pressure created against the sensors as a result of the pharyngeal wall contraction during swallowing after the bolus passed the sensor (Olsson, Nilsson, et al., 1995), and intrabolus pressure, which is the pressure created against the sensor as a result of the bolus surrounding it when the pharynx is distended prior to the contraction wave (Brasseur & Dodds, 1991; Olsson, Nilsson, et al., 1995). Thus, the occurrence of intrabolus pressure can only be identified under VFSS examination. Contact pressure is frequently reported in the literature, as it does not require VFSS, and hence, exposure to radiation. When introducing a bolus with high viscosity (Olsson, Nilsson, et al., 1995) and potentially bolus of a large volume, UES nadir pressure might be elevated in comparison to a thin or small bolus due to intrabolus pressure created by the bolus passage along the sensor (Olsson, Nilsson, et al., 1995).

Studies have investigated the relationship between pressure events recorded by manometry and the biomechanical events recorded by VFSS. For example, UES relaxation as registered by the manometer occurred at the peak of laryngeal elevation on VFSS (Olsson, Nilsson, et al., 1995). Another study found a positive correlation between high pressure detected by manometry and the presence of contact between posterior and anterior structures in the pharynx detected in an anterior-posterior view in VFSS, for sensors located at the base of the tongue and 3 cm below it, at the hypo-pharynx. In addition, increased pressure was correlated with decreased residues. The same study revealed that increased duration of the pressure events is correlated with decrease contact between the pharyngeal structures and increased (Pauloski et al., 2009).

Pharyngeal pressure measurements have been made during regular saliva swallowing (Butler et al., 2009; Doeltgen, Witte, Gumbley, & Huckabee, 2009; Hiss & Huckabee, 2005; Macrae, 2011; Olsson, Nilsson, et al., 1995; Robbins et al., 1992) during water swallowing (Butler et al., 2009; Witte et al., 2008) and during swallowing manoeuvre performance including effortful swallowing (Bülow, Olsson, & Ekberg, 2002; Hiss & Huckabee, 2005; Huckabee et al., 2005), tongue hold (Lazarus, Logemann, Song, Rademaker, & Kahrilas, 2002) and Mendelsohn manoeuvre (Lazarus et al., 2002). Normative data for pharyngeal pressure events have been collected from healthy participants (Castell & Castell, 1993; Olsson, Nilsson, et al., 1995) and several studies describe the use of pharyngeal manometry in dysphagic patients for assessment of dysphagic patients (Lazarus et al., 2002; Olsson, Castell, Castell, & Ekberg, 1995). However, comparing results between studies and between subjects is not straightforward since different studies utilized

catheters with different specifications. For example, studies have used different catheter diameters of 2.1cm (Butler et al., 2009; Huckabee et al., 2005) and 4.6 cm (Olsson, Nilsson, et al., 1995), a different number of sensors including two (Pauloski et al., 2009) and three sensors (Butler et al., 2009; Huckabee et al., 2005); and different distances between the sensors. Since the location of the sensors is fixed with the lower sensor serving as the anchoring point, the location of the top sensors might be different from person to person depending on their anatomy. For example, an MRI study found that males have longer vocal tract than females (Fitch & Giedd, 1999). Subject height can translate to pharyngeal length and, thus, tall subjects are more likely to have a longer pharynx. Consequently, the pharyngeal sensors can be located at lower anatomical positions in taller subjects as compared to shorter subjects (Butler et al., 2009).

Pharyngeal manometry has been used to document age and gender differences in pressure generation with a trend towards decreased pressure with advanced age and longer UES opening for woman than men (Robbins et al., 1992). In addition, bolus size and viscosity can alter the pharyngeal event (Butler et al., 2009; Cook et al., 1989). An increase in bolus volume causes earlier onset of swallowing events, like hyolaryngeal excursion, submental muscles activity (measured with sEMG), and UES opening, which demonstrates readiness for bolus acceptance (Cook et al., 1989).

It has been shown that pharyngeal contraction can be voluntarily manipulated with regards to its pressure amplitude and duration by execution of swallowing manoeuvres among healthy subjects (Doeltgen, Witte, et al., 2009; Hiss & Huckabee, 2005; Steele & Huckabee, 2007; Witte et al., 2008) and dysphagic subjects (Bülow, Olsson, & Ekberg, 2001; Lazarus et al., 2002) and these changes to pressure and duration can be measured by manometry.

2.5 Clinical trials – Phases

A *clinical trial* is defined as a prospective study which compares the effect and value of one or more interventions to a control condition in human beings (Friedman, Furberg, & DeMets, 2010). Clinical trials may include either diagnostic, screening, prevention, quality of life, or treatment procedures (Friedman et al., 2010), and are designed to improve patients' outcome (Steeves, Zariffa, & Kramer, 2011). The model of clinical outcome research was first introduced by the WHO in 1975 (World Health Organization, 1975), and includes several phases of research that need to be addressed prior to achieving the ultimate goal – a randomized and double-blind clinical-trial – which is the last phase of the trial (Friedman et al., 2010).

In the area of communication disorders, several papers have discussed the need for employing a comprehensive model in designing and developing interventions (Robey, 2004a; Robey &

Schultz, 1998; Rosenbek, 1995). Most of the published literature regarding the effects of long-term interventions for dysphagia bypasses important steps required to develop the optimal intervention and its assessment of efficacy (Rosenbek, 1995). Evaluation of treatment *efficacy* is the first step in developing treatments. It includes assessing the effects of the treatment on the determined outcome in an ideal setting, which allows the researcher to rule out alternative causes for the documented changes. These ideal conditions include specific and consistent implementation of the treatment, and control of any confounding variables, using valid and reliable outcome measures, etc. Efficacy studies can therefore allow for an assessment of the maximized response for the treatment (Robey, 2004a; Rosenbek, 1995). After establishing treatment efficacy, the second step is to assess treatment *effectiveness* when the treatment is implemented in a real clinical setting (i.e., the ideal conditions are unlikely to still hold). Unfortunately, overlooking the first step of efficacy assessment is quite common in the area of dysphagia research. Investigating the efficacy of treatment protocols is expensive and raises ethical considerations. It requires the undertaking of careful and structured research approach. However, omitting the stage of treatment efficacy assessment, and investigating only the treatment effectiveness, raises even bigger ethical dilemmas and budget considerations, since providing a treatment with no proven benefit to a patient is with disagreement with the code of ethics (American Speech-Language-Hearing Association, 2010). Existing research into the cumulative effects of swallowing rehabilitation techniques has largely been executed without this structured approach.

Robey (Robey, 2004a) offered a five phase model for clinical research in communication disorders which was adapted from a model offered by the National Cancer Institute. The objectives of *Phase I* are to develop research hypotheses, assess safety, develop a first approximation of the treatment protocol, estimate dose and measure the magnitude of the treatment effects. Estimation of the effect size should be performed to allow researchers to evaluate if a treatment holds a potential for causing change and the size of expected change (Robey, 2004b). Several questions can arise during this phase. What is a good enough outcome? How can observed changes affect the patients' lives? What type of population will the treatment be suitable for? The nature of this exploratory phase allows for a more flexible tolerance for Type I and II errors, thus existing effects can be better detected. It usually includes a small number of participants without a control group. Phase I research usually includes healthy participants, but may also include patients that failed to improve following existing therapy (Steeves et al., 2011). It is essential to support and justify continuation to later phases, which involve more participants and greater financial investment (Steeves et al., 2011). The goals of *Phase II* include creating and refining treatment protocol and methods, determine the optimal dosage (duration, schedule etc.), determine discharge criteria, assessing various factors that might influence the outcome,

validating the measurement instrument and refining the hypothesis. It usually involves a small sample size that is taken from the targeted clinical population. Phase II can be controlled or uncontrolled (Steeves et al., 2011). *Phase III* aims to test the hypothesis formulated in phase I and II, involves a bigger sample size, and compares the results to a control group. Together, Phases I–III tests the treatment efficacy. *Phase IV* aims to test the treatment effectiveness in a clinical setting and includes a large sample size of the targeted population with matching controls. *Phase V* occurs after the treatment has been in use in clinical setting and includes consumer satisfaction, cost-benefit analysis and quality of life assessments (Robey, 2004a; Robey & Schultz, 1998). This model offers an organized way for developing clinical-outcome research and achieving optimized intervention. Existing research into the cumulative effects of swallowing rehabilitation techniques has largely been executed without this structured approach.

PART II: SKILL VERSUS STRENGTH IN SWALLOWING TRAINING

CHAPTER 3: LITERATURE REVIEW – MOTOR LEARNING

In this chapter, the effects of two types of motor learning are discussed: skill learning and strength learning, first in the context of limb movements, and later in the context of swallowing training.

Learning has been defined as experience-dependent generation of enduring internal representations, or modification in such representation (Cohen, 1999, p. 17). *Motor learning* is an internal process that represents the current capability for producing a particular movement (R. Schmidt & Wrisberg, 2008, p. 11).

Active exercise can modify motor behaviour through the process of motor learning. Different types of training: skill, strength, endurance or power training, introduce different motor demands during training, and will therefore result in distinct adaptive changes (Adkins, Boychuk, Remple, & Kleim, 2006; Chhabra & Sapienza, 2007) at the neural level (Karni et al., 1995) and/or muscular level (Folland & Williams, 2007). Rehabilitation and treatment programmes utilize motor exercises to facilitate improvement in movements controlled by the corticospinal tract, such as limb movement (Folland & Williams, 2007) and in corticobulbar controlled behaviours, such as swallowing function (Clark 2003).

3.1 Strength training

3.1.1 Strength training of corticospinal skeletal muscles

Strength training is defined as resistance exercise resulting in an increase in force capacity (Adkins et al., 2006). Griffin & Cafarelli (2007) suggested that strength training induced another type of learning – ‘strength learning’, during which the trainee learns to increase the muscle force.

Strength training can have three goals: increased force, increased endurance, and increased power. Each of these goals can be targeted using different training activities (Clark, 2003). *Force* or *strength training* aims to increase the ability to produce large forces in one single contraction, and is characterized by high level resistance exercise (Kisner & Colby, 2007). *Endurance training* aims to increase the ability to produce sustained or repeated forces over an extended time period, and is characterized by low level resistance exercise (Kisner & Colby, 2007). *Power training* increases the ability to produce force at high speed and includes exercises that utilize low to

moderate forces of high contraction velocities (Clark, 2003; Kisner & Colby, 2007; Moffroid & Kusiak, 1975).

Muscle strength is a result of its (1) physiological strength (cross-sectional area, muscle density and size), (2) neural strength, meaning the communication between the CNS, motoneuron and the muscle, and (3) mechanical strength (the angle and length of its lever and joint characteristic) (Folland & Williams, 2007). Strength training influences each of these levels.

Strength training results in both neural adaptation and morphological changes (Folland & Williams, 2007). These changes occur in a timed manner. First, there is an increase in voluntary neural drive which accounts for an apparent increase in strength, followed by an increase in muscle size accompanied by continuation of neural adaptation, with hypertrophy being the dominant factor that accounts for increased strength later in training (Burkhead et al., 2007; Moritani, 1993).

When performing a motor activity, a motor plan that includes information regarding motoneuron recruitment patterns, is created to activate specific muscles. Neural adaptation occurring following strength training will result in improvement in the efficiency of motor unit recruitment patterns which are controlled by the CNS (Barlow, 1999). Changes in the number and coordination of the motor units recruited will occur, and affect muscle function, resulting in increased force and precision of the movement (Burkhead et al., 2007; Clark, 2003).

Briefly, a motor unit is composed of an alpha motor neuron and the muscle fibres it innervates. Two groups of motor units exist in skeletal muscles. *Type I units* are resistant to fatigue, slow twitching and are capable of producing small tension. *Type II units* are fast twitching that are able to produce large forces. Type II units are further subdivided to *fast fatigable units* which are able to produce large tension and fast to fatigue; *fast resistant units* that are resistant to fatigue and can produce medium tension. These motor units are recruited in an orderly manner, starting with the ones that can produce small forces (Type I), followed by units that produce moderate forces (Type II – fast resistant), and finally those producing large forces (Type II – fast fatigable). Recruitment pattern of those units will depend on the type of exercise and the force required during it, and those will be determined by the specific behaviour targeted (Clark, 2003; Folland & Williams, 2007). de Lateur (1996) found that muscle fatigue following motor exercise will cause recruitment of Type I (slow twitching) and Type II (fast twitching) motor units and will therefore improve both strength and endurance.

In addition to changes in motor unit recruitment patterns, strength training also enhanced the motor unit firing rate, leading to earlier motor unit activation onset, and decreased time lag

between firing spikes throughout the EMG burst (Van Cutsem et al., 1998). These changes in the firing rate increased the maximum contraction capacity and the speed of force development.

Neural adaptations account for an increase in strength in the early stages (first 2 weeks) of strength training, in the absence of muscle hypertrophy (Folland & Williams, 2007; Moritani & DeVries, 1979). For example, intensive weight training resulted in significant improvement in strength without a measurable change in muscle circumference (Komi, 1986). In another study, an increase in strength as measured by sEMG, was documented after 4 weeks of training (Häkkinen & Komi, 1983).

Studies that found cross-over training effects provide *indirect* evidence for the occurrence of neural adaptations (Zhou, 2000), whereas studies that found changes in MEPs provide *direct* evidence for those (Griffin & Cafarelli, 2007). Documentation of increased strength in the contralateral, untrained limb (Moritani, 1993) is an example of cross-over effects. The underlying hypothesis for the occurrence of cross-over effects is that during strength training, new or existing activation synergies, comprised of antagonist and agonist muscles, are being created or re-enforced. This involves coordination of the movement itself together with activation of other stabilizing muscles during particular task. This learned pattern of action is stored within the CNS, and therefore, could be utilized for the contralateral untrained limb (Gandevia, 2001; Rutherford & Jones, 1986). Imagined training can also cause increases in strength. Zijdwind et al. (2003) found a greater increase (+36%) in maximal torque production after 7 weeks of imagined contractions of the ankle planter-flexor in comparison to low intensity training (+13%). It can be argued though, that imagined strength training, might be considered as skill training since it requires increased amounts of movement planning, storing the information and creating a new motor plan.

Remple, Bruneau, VandenBerg, Goertzen, & Kleim (2001) examined the effects of power-reaching training (strength task) versus non-power-reaching training task (skill task) in rats. They found that both training groups exhibited the same cortical reorganization patterns, thus the element of increased power did not make a difference, but rather the skill involved in learning the reaching task was the element that led to change at the neural level. However, in a later paper from the same group, Adkins et al. (2006) reported that the rats in the strength group had more excitatory synapses within the spinal cord compared to the rats in the skill training group and to the non-training control rats; however, the number of inhibitory synapses did not differ between groups. This increase was suggested to account for the increased strength that was evident in the strength groups in comparison to the other groups and might indicate a possible decreased recruitment threshold of the motor units. Carroll, Riek, & Carson (2002), Jensen, Marstrand, & Nielsen (2005) and Griffin & Cafarelli (2007) documented the effects of isometric resistance

training of limb muscles on cortical excitability in humans. Both Carroll et al. (2002) and Jensen et al. (2005) found a decrease in MEP magnitude following strength training of the upper limb. Carroll et al. (2002) found a decrease during muscle contraction and Jensen et al. (2005) – during rest, in addition to a non-significant reduction during contraction. This decrease might be a result of changes in the firing rate of the spinal motoneurons or due to changes to their intrinsic firing properties (Carroll et al., 2002) but can also indicate a possible change in cortical or spinal neuron excitability and the synaptic connection between them (Jensen et al., 2005). In contrast, Griffin & Cafarelli (2007) found an increase in corticospinal excitability following 4 weeks of resistance training of the anterior tibialis muscle (lower limb), as evidenced by increased MEP amplitude that occurred as early as the 6th day of training and remained high at 4 weeks into training. This increase was assumed to represent neural adaptations to repeated forceful contractions, as opposed to the nature of neural adaptations that accompany learning of a new task, which are characterized by increased excitability in the early stages of learning followed by a later decrease in excitability (Karni et al., 1995; Muellbacher, Ziemann, Boroojerdi, Cohen, & Hallett, 2001). The higher excitability documented in Griffin & Cafarelli (2007) could be a result of higher firing rates and lower recruitment thresholds of the motor units as suggested by the authors. It was proposed that strength training leads to creation of a motor plan for executing high-level contractions due to the effects of ‘strength learning’. This motor plan allows coordinated and efficient synergetic activation of large forces (Burkhead et al., 2007; Griffin & Cafarelli, 2007) by maximizing agonist muscles activation, increasing stabilizing muscles activation that create antagonist contraction, and reducing activation of antagonist muscles (Folland & Williams, 2007; Kidgell & Pearce, 2011; Sale, MacDougall, Upton, & McComas, 1983). The discrepancy in results regarding the effects of strength training on neural excitability might be a factor of the muscle being trained. It is possible that training of the anterior tibialis muscle resulted in increased MEPs magnitude (Griffin & Cafarelli, 2007), as opposed to decreased MEPs following training of index finger abductors (Carroll et al., 2002) and biceps brachii (Jensen et al., 2005), due to differences in muscle size, with bigger muscles requiring more firing of motor units and more time to develop neural adaption in response to strength training.

Morphological adaptations following strength training include myofibrillar (the basic unit of the muscle) growth, both in size and in numbers, presenting as muscle hypertrophy, which is manifested by an increase of the cross sectional muscle area. Satellite cells located around the muscle fibres undergo mitosis and become myonuclei that produces proteins which fuses with the muscle fibres, and therefore contribute to the hypertrophy (Folland & Williams, 2007). This enlargement in muscle size affects the force generation capacity of the muscle and is the desired goal in strength training (Powers & Howley, 2001). Other morphological changes include changes in fibre type during the first 2-3 month of training (McCall, Byrnes, Dickinson, Pattany, & Fleck,

1996a; Williamson, Gallagher, Carroll, Raue, & Trappe, 2001). There is a shift towards an increase in the proportion of Type I fibre muscles (Burkhead et al., 2007) that are characterized by slow contraction and are fatigue resistant due to efficient ATP production. ATP is the energy source that enables contraction (Powers & Howley, 2001). In addition, mechanical adaptation includes an increase in tendon stiffness (Kubo, Kanehisa, & Fukunaga, 2001).

Several variables affect muscle hypertrophy. The cross-sectional area of the muscle was found to increase differentially following high-resistance strength training depending on the muscle group (upper or lower extremity). For example, the cross-sectional area of the elbow flexor muscles increased by $22\% \pm 4\%$, whereas the knee flexors increased by only $8\% \pm 2\%$ in young participants who underwent 3 months of progressive resistance training (Welle, Totterman, & Thornton, 1996). It is possible that this finding is related to differences in MEP size between upper and lower extremities reported above, with upper extremities reacting faster to strength training and showing more hypertrophy than lower extremities. Another variable that influences muscle hypertrophy is gender, with men exhibiting a 2.5% greater increase in cross-sectional area of muscles than women, after 12 weeks of training. Women, on the other hand, manifested greater gains (+25%) in dynamic strength and in isometric strength (+6%) when compared to men (Hubal et al., 2005). However, this finding is not consistent across all studies (Roth et al., 2001; B. L. Tracy et al., 1999). Age can also influence muscle hypertrophy. Even at the age of 85-97 years, the cross-sectional area was found to increase by almost 10% after 12 weeks of strength training of the knee extensors (Harridge, Kryger, & Stensgaard, 1999). However, some authors suggest that older participants had less change than young in response to strength training (Häkkinen et al., 1998; Welle et al., 1996) and some indicate no age effect (Roth et al., 2001).

The results of strength training on stroke patients as a rehabilitation approach introduces a new criterion for evaluating efficacy by measuring carryover effects to functional activities. Van Peppen et al. (2004) reviewed the evidence for the impact of physiotherapy on stroke patients. They found that strength training approaches can improve the strength and range of motion of the targeted muscles; however, this improvement does not carry-over into functional tasks like walking endurance or dexterity. One of their conclusions was that impairment-focused programmes do not generalize to functional improvement, as opposed to exercises programmes in which the functional training goal or behaviour is utilized to serve as the training task. Morris et al. (2004) conducted an electronic database search for studies conducted between 1996 and 2002, and found that out of 8 randomized controlled trials that measured the effects of resistance training following stroke, only 3 documented carry-over effects and functional improvement. Lack of carryover found in the other studies might be due to the duration of the training period (2 weeks versus 4 weeks), its frequency (twice a week versus five times a week), impairment

severity, and participant's age (Morris, Dodd, & Morris, 2004). For example, in a randomized, controlled trial, strength training aiming to increase the static force production of the upper limb resulted in improved strength of the trained limb, however no functional improvement were documented. Lack of improvement might have been due to reduced incorporation of the paretic arm into functional activities, outside of the training session, or due to insufficient improvement in strength (Bourbonnais et al., 2002). In contrast, another randomized, controlled trial that consisted of upper-limb training following stroke (Bütefisch, Hummelsheim, Denzler, & Mauritz, 1995) documented functional improvement. This study aimed to increase the speed of movement and to increase force during flexion and extension while reducing muscle tone. Improvement might have been related to the high repetition rate of the exercise or due to emphasising the velocity component rather than force component solely.

To summarize, following strength training there are early neural adaptations followed by structural adaptations that include two types of morphological changes: hypertrophy and fibre type shifts, and mechanical change of increased stiffness of tendons. This body of evidence regarding adaptations following strength training was based on the healthy population. Rehabilitation research documented changes at the activity level following strength training that involved the targeted behaviour.

3.1.2 Strength training in swallowing rehabilitation

Most of the literature regarding strength training has focused on muscles of the limbs but there is also evidence for the effects of strength training in swallowing. Most approaches in swallowing rehabilitation consist primarily of strength training. These methods are presumed to generate safer and more efficient swallowing by strengthening oropharyngeal muscles (Burkhead et al., 2007).

Swallowing requires submaximal muscle activity (Burkhead et al., 2007), thus one may presume that in the presence of weakness, this activity will not be affected. However, a disruption in muscle activation resulting in force reduction will decrease the *functional reserve* of the muscle, meaning the difference between the force needed to perform an action and the maximal force generation capacity of that muscle. A reduction in muscle reserve will lead to rapid muscle fatigue and an increase in perceived effort by the individual (Burkhead et al., 2007). Age-related decrease in muscle reserve was found in tongue muscles (Nicosia et al., 2000). Reduction in muscle reserve is also manifested in changes in swallowing physiology documented in older subjects, such as prolonged bolus transit, and reduced UES opening (Logemann et al., 2000; Robbins et al., 1992). Age-related decreases in muscle strength might put older subjects at increased risk for dysphagia in case of a further reduction in muscle reserve (e.g., following lengthy hospitalization).

Reduction in muscle strength is also seen following damage to the LMN, UMN or neuromuscular junction. In addition, muscle weakness cannot only result in a decrease in muscle force but also in a reduction in range and speed of motion (Clark, 2003; Luschei, 1991).

Swallowing rehabilitation techniques are targeted at restoring the underlying impairment by either addressing the swallowing process itself (Robbins et al., 2008), using techniques such as Mendelsohn manoeuvre (Logemann & Kahrilas, 1990), effortful swallow (Bulow, Olsson, & Ekberg, 2001), and tongue hold (Fujiu & Logemann, 1996), or by addressing the muscles outside the context of swallowing, with head lifts (Shaker et al., 1997) and lingual exercise (Robbins et al., 2005). All of these exercises increase the effort, duration, and force of the muscles involved in swallowing. The effects of these techniques are supported by some evidence from the literature regarding their influence on swallowing biomechanics (Bulow et al., 2001; Hiss & Huckabee, 2005; Shaker et al., 1997) and muscular hypertrophy (Robbins et al., 2005). Since rehabilitation, by definition, should lead to enduring effects, the long-term effects of swallowing-related strength training are of interest. However, most of these behavioural exercises have been evaluated for their immediate effects. Long-term effects have only been evaluated for the McNeill dysphagia therapy programme, two swallowing training exercises performed outside the context of swallowing (tongue strengthening and head-lift manoeuvre); and two non-swallowing related exercise (EMST and LSVT). In addition, Macrae (2011) documented the cumulative effects of 6 weeks of the modified head-lift exercise and effortful-swallowing rehabilitation techniques. The results from these studies are presented and discussed below. Studies documenting the cumulative effects of effortful swallowing are discussed in Section 3.1.2.1.2 *Cumulative effects of effortful swallow*.

Robbins et al. (2005) examined the effects of an 8-week lingual resistance exercise programme. Ten healthy older participants (70-89 years old) compressed an air-filled bulb held between the tongue blade and the hard palate, using the IOPI for 8 weeks. Training was accompanied by visual biofeedback from the device regarding the precise pressure, and light signals indicated success. Robbins et al. saw an increase in both swallowing pressure and isometric tongue pressure as measured with oral pressure sensors, paired with an increase in tongue volume by an average of 5.1% and range of 2.2–10.7%, as measured with MRI (n = 4). Robbins et al. (2007) then measured the effects of the same lingual exercise in 10 stroke patients with dysphagia (51-90 years old). They found that after 8 weeks of 10 repetitions completed 3 times a day, 3 days a week, there was a significant increase in isometric pressure that translated to improved swallowing function as measured by VFSS. However, not all measures were improved. Pharyngeal residues decreased significantly but there was no reduction in oral, cricopharyngeal, piriform sinuses, and vallecula residues. Aspiration-penetration scale score improved for the

liquid bolus but not for the semi-liquid bolus. Two of the three participants who underwent MRI, showed hypertrophy of the tongue with an average increase of 4.3%. The third one showed a decrease that was related to reduce oral intake and depression. These results indicate that improvement in tongue strength is possible following training in healthy and dysphagic subjects, and the increase in strength can carry-over into swallowing behaviour. However, carry-over did not extend to all swallowing conditions.

Another strength training exercise was examined by Shaker et al. (1997). They compared the result of a head-lift exercise to a sham exercise, following 6 weeks of training, 5 days a week. The results showed an increase in anterior laryngeal excursion, greater opening of the UES during swallowing in its anterior-posterior diameter and an increase in the UES CSA during opening. The same group (Shaker, Easterling, et al., 2002) measured the effects of the same exercise, performed at the same intensity, in 27 dysphagic patients with abnormal UES opening, and found an increase in the anterior-posterior diameter of the UES during opening but not in the lateral diameter of UES during opening. Interestingly, there was no significant difference ($p = 0.4$) between the head-lift group and a sham group in anterior-posterior diameter of the UES. Other than this report, it is not clear which of the results were based on between-groups analysis and which were based on pre- vs. post-treatment data. Increased anterior laryngeal excursion was documented, but no significant changes occurred in the superior aspect and also no significant changes occurred in anterior and superior hyoid excursion. Improvement in functional swallowing was documented as measured by a scale of swallowing competency. Post-swallow pyriform sinus residues decreased and post-swallow aspiration decreased as well (Shaker et al., 2002). In another study, the effects of head-lift training ($n = 5$) were compared to traditional training ($n = 6$) of the Mendelsohn manoeuvre, tongue strengthening, etc. Following both types of training protocols, no changes in residue occurred, but the head-lift group showed reduced post-swallowing aspiration. Traditional treatment resulted in increased superior hyoid movement and superior and anterior laryngeal movement in some textures, while head-lifts improved only UES opening diameter (Logemann et al., 2009). Again, it is not clear which of the reported results consist of differences between groups or differences within group. It is not clear whether or not head-lift training influences anterior laryngeal elevation due to contradictory reports. Also, lack of difference between sham and head-lift groups in UES opening raises questions regarding head-lift effects on the UES, although the improvement in post-swallow pyriform sinus residues and aspiration following head-lifts provide some support (Shaker et al., 1997).

Macrae (2011) documented the cumulative effects of the modified head lift protocol in healthy adults. The modified protocol consisted of 30 isokinetic head-lifts and three isotonic head lifts, each 30 s long. The subjects performed the exercise at home and completed a log sheet.

Assessments performed before and after the training period, included pharyngeal manometry for assessing pharyngeal and UES pressures events, submental activity using sEMG, submental muscles ultrasonography for assessing the CSA and hyoid displacement, and TMS for assessing submental MEPs. No changes in any of the measures were present following training. Small training effects may have been present but could not be detected due to the high variability of the data.

Non-swallowing-related exercises have been found to improve swallowing function in dysphagic participants. EMST aims to increase maximal expiratory pressure generation by using a one-way valve with adjusted resistance to air flow. Pitts et al., (2009) examined its effects in ten participants with PD and aspiration or penetration, demonstrated in VFSS examination, who went through 4 weeks of training. Improved voluntary cough function and decreased penetration and aspiration scores were present following training. Troche et al. (2010) examined its effects in a randomized sham-control trial of 60 subjects with dysphagia secondary to PD. Subjects in the training group trained for 4 weeks using the one-way valve, which was set on a weekly basis with a load of 75% of the maximal expiratory pressure. Subjects in the sham group used a sham valve that introduced no load. There was a significant difference between groups, with the EMST group demonstrating less penetration/aspiration of a bolus and an increase in hyoid displacement during UES opening and closing, demonstrated during VFSS examination. These changes allow improvement in bolus flow through the UES leading to improved pharyngeal clearance. Increased submental activity is likely to be the underlying mechanism leading to the changes mentioned above. LSVT is a programme designed to improve the perceptual characteristics of voice in people with PD. El Sharkawi et al. (2002) reported improvements in the function in both the oral tongue and the tongue base during the oral and pharyngeal stages of swallowing following training in eight patients with PD and dysphagia. Dysphagic symptoms included the oral phase, including oral preparation and oral transit phase. Base of tongue retraction, anterior to posterior tongue movement, and onset of pharyngeal swallow improved or resolved. In addition, there was delayed laryngeal vestibule closure, which occurred often before training and did not change after training. Aspiration was not present prior to treatment or after it. Thus, oral phase difficulties were reported to improve, however pharyngeal phase difficulties remained. In addition, although not specifically indicated in the paper, dysphagia characteristics appeared to be mild or moderate, considering the fact that no aspiration occurred. In summary, LSVT improved oral phase dysphagia, with no affect on pharyngeal phase dysphagia, in patients with overall mild-moderate dysphagia.

Most swallowing exercises are impairment-focused. They target a muscle or a group of muscles that participate in swallowing but do not utilize the swallowing process itself during exercise. Van

Peppen et al. (2004) commented on the importance of using the targeted behaviour during training but the current literature lacks studies incorporating function-focused training aimed at increasing strength. The next section includes discussion of strength training principles that promote motor learning in swallowing training.

3.1.2.1 *Effortful swallow*

Effortful swallow is a commonly used swallowing manoeuvre (Lazarus, Logemann, Song, Rademaker, & Kahrilas, 2002) that was first described by Kahrilas and colleagues as a compensatory technique (Kahrilas, Lin, Logemann, Ergun, & Facchini, 1993; Kahrilas, Logemann, Krugler, & Flanagan, 1991; Kahrilas, Logemann, Lin, & Ergun, 1992). Its aim is to increase the motion of the posterior base of tongue towards the posterior pharyngeal wall in order to improve bolus clearance from the vallecula (Logemann, 1988) and, thus, generate increased pressure to propel the bolus through the upper pharynx (McConnel, 1988). Instructions regarding performance vary slightly between papers: “Swallow very hard while squeezing the tongue up and back toward the soft palate” (Bülow et al., 2002) and “As you swallow, squeeze hard with all of your muscles” (Logemann, 1998, p. 221). Later, it was reported as a rehabilitation technique used in clinical settings in order to create safe bolus passage and reduce aspiration (Bryant, 1991; Carnaby-Mann & Crary, 2010; Crary, 1995; Huckabee & Cannito, 1999).

Effortful swallowing is widely investigated in the literature (Wheeler-Hegland et al., 2009) and is one of the five most widely-documented swallowing-specific manoeuvres as stated by Wheeler-Hegland et al. (2008). Studies have documented its effect on swallowing biomechanics in healthy and dysphagic subjects. However, the focus of most of the literature has been on the immediate changes during execution of the task, with only a few studies focused on its cumulative effects.

3.1.2.1.1 *Immediate effects of effortful swallowing*

Studies that evaluated the short-term effects of effortful versus non-effortful swallowing, identified influences on submental muscle activity, tongue pressure, duration and peak pressure in the pharynx and in the UES and hyoid movement. However, there are inconsistencies in the literature.

Effortful swallowing has been found to be accompanied by increased *sEMG amplitude* as measured from a midline location over the submental muscle group, including peak sEMG, average sEMG amplitude and maximum amplitude at maximum hyoid displacement in comparison to normal swallow (Wheeler-Hegland et al., 2008), supporting the findings of Huckabee, Butler, Barclay, & Jit (2005) regarding increased sEMG amplitude from the same

location. Huckabee & Steele (2006) identified that submental sEMG amplitude was heavily influenced by intrinsic tongue muscles activity. Thus, during effortful swallow, intrinsic tongue muscles participate and influence the sEMG activation recorded from the submental muscles. However, it is possible that both increased tongue pressure and increased submental activation co-occur during effortful swallowing, thus, association rather than causality might be the reason for increased submental sEMG amplitude.

Swallowing-related tongue pressure was found to increase during effortful swallow in comparison to non-effortful, in healthy 45-93 years old subjects, as measured with oral bulb pressure sensors located in the oral cavity (Hind, Nicosia, Roecker, Carnes, & Robbins, 2001). The difference between effortful and non-effortful swallows is larger in young subjects in comparison to older subject as a result of decreased maximal oral pressure in older subjects (Hind et al., 2001). Several studies have investigated the effects of effortful swallowing on tongue pressure in dysphagic laryngeal cancer patients. An increase in tongue pressure during effortful swallow was documented using a pressure sensor located between tongue base and pharyngeal wall (Lazarus et al., 2002). Another study found that tongue pressure amplitude values reached those reported for healthy adults when performing a non-effortful swallow (Castell & Castell, 1993). However, time duration of the tongue pressure event was still shorter in dysphagic than in healthy adults (Yokoyama, Mitomi, Tetsuka, Tayama, & Niimi, 2000). An interesting result from Huckabee & Steele (2006) was that increased tongue-palate pressure during effortful swallow is associated with increase pharyngeal pressure. During effortful swallowing, there is co-occurrence of increased tongue pressure, increased EMG amplitude from the submental muscle group, and increased pharyngeal pressure. Thus, effortful swallowing might create an overall increased activation of muscles involved in swallowing, rather than a specific increase in a certain area, although its intended aim was to increase tongue pressure and contact between the tongue base and posterior pharyngeal wall (Logemann, 1998).

The literature evaluating the effect of effortful swallow on *hyolaryngeal elevation* is in disagreement. Bulow, Olsson, & Ekberg (1999) studied healthy participants ($n = 8$) and found that, at the pre-swallow phase while the subjects were preparing to perform effortful swallow, the hyoid and larynx were already elevated. This caused a substantial reduction in the relative change of hyolaryngeal elevation during swallowing, a finding which raised some concerns (Huckabee & Steele, 2006), since hyolaryngeal excursion plays an important role in swallowing. To further investigate this point, Hind et al. (2001) studied a larger group ($n = 64$) and found that the effortful swallow influences hyoid movement by increasing the superior movement by 17.7 mm (SD 4.4 mm) but reduces the anterior movement by 5.6 mm (SD 6.3 mm) in comparison to non-effortful swallow. In addition, the duration of the anterior movement was longer during effortful

swallow. It is possible that if the hyoid bone had been measured at complete rest, before the subjects received the instruction to prepare to perform an effortful swallow, the overall distance of displacement would have been within normal range. However, the pre-elevation might have negative effects on swallowing biomechanics. In contrast to reports regarding reduced excursion, no differences were found in effortful swallow patterns of hyoid elevation and displacement in comparison to non-effortful swallow in Wheeler-Hegland et al. (2008) study. The difference between the results might be explained by differences in the ages of their subjects: Bulow et al. (1999) – 25-64 years; Hind et al. (2001) – 45-93 years; Wheeler-Hegland et al. (2008) – 18-35 years. In the presence of intact swallowing mechanisms, young participants may be less capable of changes in hyoid displacement due to physiologic constraints that enable the hyoid bone to move only by a certain optimal amount sufficient for successful swallowing, as Wheeler et al (2008) have suggested. In addition, it is possible that in Wheeler-Hegland et al. (2008) study, the hyoid was measured from complete rest rather than the point of preparing of performing effortful swallowing.

Huckabee et al. (2005) found that effortful swallow increases *pharyngeal pressure* in healthy participants more at the mid-pharynx than upper pharynx, but increased duration of pharyngeal pressure more in the upper pharynx than mid-pharynx (Hiss & Huckabee, 2005). However, in contrast, Witte, Huckabee, Doeltgen, Gumbley, & Robb (2008) found increased duration in mid-pharynx but not at upper pharynx. The negative correlation between amplitude and duration found in another study (Pauloski et al., 2009) might explain these findings of decreased peak amplitude associated prolonged time duration. In contrast to the Huckabee studies (Hiss & Huckabee, 2005; Huckabee et al., 2005), Bulow et al. (1999) found no difference in pharyngeal pressure and duration at the level of inferior constrictor muscle between effortful and non-effortful swallow in healthy participants. This finding was later supported and expanded by Witte et al. (2008) who found no difference in peak pressure between effortful swallows of saliva and water to non-effortful swallows of the same type of boli. Hence, the influence of effortful swallowing on pharyngeal pressure is not clear. Hind et al. (2001) hinted at the possibility of adverse effects in healthy participants, with a correlation between increased pyriform sinuses residue during effortful swallow with increased age, indicating a possibility of decreased pharyngeal pressure, or possibly negative effects on the coordination of swallowing in older subjects leading to residue. This possibility of reduced coordination has yet to be explored, and would be of importance for choosing rehabilitation programmes for people with dysphagia.

Hiss & Huckabee (2005) found that during effortful swallow there is a longer time gap between the onset of the EMG activity from the submental muscle area and the onset of the manometric events in the pharynx. However, in a study conducted later by Steele & Huckabee (2007), a

different method of analysis was used and instead of measuring the onset, the peak amplitude was used as a reference point for durational measurement, which revealed that effortful swallow led to a shorter time gap between the EMG peak and pharyngeal peak. This finding supports the role of effortful swallow in generating faster bolus propagation into and through the pharynx.

The results of studies of effortful swallow in dysphagic patients are also conflicting. Bulow et al. (2001) found a decrease in pharyngeal pressure during effortful swallow and also found that one patient with severe dysphagia had greater pharyngeal retention while performing effortful swallow, which might support the findings of Hind et al. (2001) regarding increased residue at older ages. However, Lazarus et al. (2002) found less pharyngeal residue in comparison to non-effortful swallow in dysphagic patients treated for laryngeal cancer, a finding which supports Huckabee et al. (2005) findings in healthy participants, and indicates better pharyngeal clearness. It is likely that the negative results reported by Bulow et al. (2001) and the positive results reported by Lazarus et al. (2002) reflected the different causes of the dysphagia in their patients (stroke and laryngeal cancer, respectively). Stroke patients might exhibit motor planning difficulties, whereas patients treated for laryngeal cancer might have reduced pharyngeal pressure due to missing structures, thus can benefit from effortful swallowing.

UES pressure and duration were not significantly different during effortful swallow in comparison to non-effortful according to Bulow et al. (1999) in a study of healthy subjects. In addition, the maximum width of UES opening did not differ (Hind et al., 2001). However, UES opening was significantly longer during effortful swallow than non-effortful according to Hind et al. (2001) and Hiss & Huckabee (2005). Lower pressure at the UES during effortful swallow was reported (Huckabee et al., 2005) during both saliva and water bolus effortful swallow, with effortful saliva swallows leading to significantly more negativity at the UES than effortful water swallows (Witte et al., 2008). The difference between water and saliva swallows might be due to intrabolus pressure of the water bolus that increased the registered pressure and the sensor (Brasseur & Dodds, 1991; Olsson, Nilsson, et al., 1995), leading to higher pressure during effortful swallowing of water relative to saliva. In post-stroke dysphagic patients, UES opening was incomplete and shorter in effortful compared to regular swallows (Bulow et al., 2001), thus indicating increased chances for pyriform sinus retention. The same studies that reported decreased laryngeal elevation also reported no influence on UES opening, thus it is possible that decreased elevation resulted in a cascade of events that are inter-related, leading to increased pyriform sinus retention. The link between UES opening and laryngeal excursion is supported by Jacob, Kahrilas, Logemann, Shah, & Ha (1989), who found a positive correlation between the negative pressure of the UES and hyoid excursion.

Concerning the different findings on pharyngeal pressure, one explanation is that the subjects in the different studies had different levels of training, and thus had different levels of performance of this technique. Witte et al. (2008) postulated that the increased pressure in the pharynx found in earlier studies (Huckabee & Steele, 2006; Huckabee et al., 2005) but not found in Witte et al.'s (2008) study might be a consequence of different mastery levels of the technique. Huckabee et al. (2005) and Huckabee & Steele (2006) used biofeedback in order to teach the subjects how to perform this technique, whereas Witte et al. (2008) did not. This might also account for Bulow et al.'s (1999) results, as they reported a very limited time of preparing their participants to perform the task. In Bulow et al.'s (2001) study, it might be that since the dysphagic participants did not implement this manoeuvre properly, its full extent of influence was not apparent. One reason for that could be that a possible decrease in muscle reserve in those dysphagic patients, led to decreased effort, range of motion, and speed of the motor events (Burkhead et al., 2007; Clark, 2003). And indeed, Bulow et al. (2001) reported on difficulties performing this technique in half (4/8) of their dysphagic participants, with weakness of the tongue muscles reported as a possible cause. In addition, adverse effects of the techniques have been reported in their more severe dysphagic subject. Adding to this point is the research by Hind et al. (2001) regarding the correlation between increased age and increased residuals in the pyriform sinus. Again, this can be explained in terms of reduction in muscle reserve and weakness in older subjects, affecting their ability to perform this technique. Effortful swallowing might require utilization of a biofeedback modality to ensure correct performance during technique acquisition. In addition, muscle strength might be required in order to execute effortful swallowing. Inability to perform the technique correctly might detract from its influence on pharyngeal pressure.

With regards to *airway protection*, research by Hind et al. (2001) suggests that with effortful swallow the airway is protected for a longer time period since the laryngeal vestibule is closed for a longer period of time. And, indeed, effortful swallow decreased the depth of contrast penetration in dysphagic participants (Bulow et al., 2001).

Lever et al. (2007) found that effortful swallow could also affect the smooth oesophageal muscles. An increase of 11 mmHg was found in the distal region of the oesophagus, adjacent to the LES. This might indicate that effortful swallow affects not only skeletal muscles but also smooth muscles that are regulated by the autonomic and somatic nervous system (Kuramoto, Kawano, Sakamoto, & Furness, 1999).

To summarize, the short-term effects of effortful swallow on biomechanics indicate increased tongue pressure reflected by oral pressure sensors and submental sEMG, decreased or unchanged anterior hyolaryngeal excursion, and increased superior elevation. Pharyngeal and UES pressure

and duration finding are in conflict, with studies indicating either increase, decrease or no change. Airway protection might be improved and there may be an increase in LES pressure.

3.1.2.1.2 Cumulative effects of effortful swallowing

The cumulative effects of effortful swallowing as an approach for improving swallowing physiology have been reported by several studies discussed below.

Huckabee & Cannito (1999) described a clinically-based study of effortful swallow utilizing sEMG as a biofeedback modality, across 10 sessions, in 10 chronic dysphagic patients. They based the prescription of this manoeuvre on VFSS, when pharyngeal contraction was either weak or disorganized, or when laryngeal excursion was reduced and resulted in vallecular or diffuse residual and inadequate epiglottic deflection. They found that 8 of their 10 patients returned to oral feeding, and 9 of the 10 improved their swallowing. However, their paper lacks details regarding the number of patients that were prescribed with effortful swallow and the number of repetitions of this technique. In addition, since this technique was used with combination of other techniques (e.g., Mendelsohn manoeuvre), specific details of the outcomes related to effortful swallowing were not available.

The McNeill dysphagia therapy programme involves effortful swallowing of different boli that are gradually increased in size, with a constructed hierarchy of swallowing tasks characterized by increased systematic load to the patient's swallowing system. Thus, this therapy programme adheres to principles of motor learning documented in the exercise physiology literature (Carnaby-Mann & Crary, 2010) which will be discussed below. The patient is instructed to swallow as hard and fast as possible, and an emphasis is given to reduce the number of swallows per bolus. Every treatment session lasts for an hour with 91 swallowing trials included; sessions are scheduled 5 days a week for 3 weeks, plus home practice. As described by the authors (Carnaby-Mann & Crary, 2010), the aim is to strengthen the muscles and improve swallowing coordination that was found to be different in dysphagic patients than healthy controls (Crary & Baldwin, 1997). It is important to point out that the latter study from the Crary group based its conclusion regarding 'less coordination' (Crary & Baldwin, 1997, p. 180) on visual examination of sEMG waveforms recorded from three muscles involved in swallowing. Coordination was based on identification of clear onset/offset and "well defined swallowing" (Crary & Baldwin, 1997, p. 182). In a case-series retrospective study by Carnaby-Mann & Crary (2010), a comparison was made between 2 groups of chronic dysphagic patients. One group (n = 16) was treated with a traditional approach that applied several swallowing manoeuvres and utilized biofeedback, and the other group (n = 8) went through the McNeill dysphagia therapy programme that used effortful swallowing of different boli. The results were that the patients in the McNeill

programme had better oral intake score, reduced aspiration risk and increased probability of feeding tube removal, in comparison to the traditional treatment group. The authors concluded that 3 weeks of intense training utilizing effortful swallow of different boli can have positive cumulative results on swallowing function biomechanics. However, this conclusion is somewhat problematic due to several confounds in the study design. Since the aim of the study was to evaluate the use of a constructed intense therapy to a commonly-used traditional therapy that uses biofeedback, the two therapy programmes were not directly comparable. Thus, this lack of uniformity does not allow for a clear, differential understanding of the factors that influenced the results. It is possible that the different intensities used in the 2 types of treatment were a crucial factor, even more important than the type of exercise used and the presence or absence of biofeedback. The traditional therapy group had on average 12 sessions, and 32 trials per session, giving a total of 384 trials. In contrast, the McNeill programme group had 19 sessions on average (which does not correspond to the authors' description of maximum 15 sessions in the same paper) with 91 swallowing trials per session, giving a total of 1739 trials and accounting for additional prescribed home exercises. Another possible factor that might have influenced the results was the patients' motivation for treatment: participants in the McNeill treatment group agreed to a 3-week study, whereas patients in the traditional therapy group were not informed of the length of their therapy. Although blinding was reported for VFSS ratings, the fact that the study was retrospective with respect to the patients in the traditional therapy group means that the researcher scoring the VFSS could have seen the differences in dates of data collection (1994 – 1999 for the traditional therapy group and 2006 – 2008 for the McNeill programme).

Macrae (2011) studied the effects of an effortful-swallowing protocol in healthy adults. The protocol involved 33 effortful swallows, performed three times daily, five days a week, for 6 weeks. The subjects performed the exercise at home and kept a log sheet. The same assessments described above were performed before and after the training period (pharyngeal and UES pressures events, submental activity, submental muscles submental CSA, hyoid displacement, and submental MEPs). No changes in any of the measures were seen following training. It is possible that changes were not found due to the occurrence of small effect sizes that were masked by inherent variability in the outcome measures. Another possibility is low compliance of the subjects prescribed with the home-based programme. It is also possible that since the participants were healthy, there was no 'room' for changes, nonetheless, other studies have employed healthy subjects and reported measurable changes (Robbins et al., 2005; Shaker et al., 1997).

The effects of effortful water swallowing on submental MEPs magnitude were tested in nine healthy young subjects. The protocol used in the study consisted of task repetitions for 15 min a day, once daily, for 1 week (Gallas, Marie, Leroi, & Verin, 2009). The results indicated an

increase in MEP magnitude following the training period. However, as pointed out by Macrae (2011, p. 253), Gallas et al. treated each data point as an independent variable, despite claiming having used repeated measures ANOVA in the text. Hence, the true effects of the Gallas et al. effortful-swallowing protocol remain unclear.

Garcia, Hakel, & Lazarus (2004) documented adverse effects of the cumulative use of effortful swallow in a case report describing a 12 year old patient post-surgical removal of a dorsal brainstem tumour. Effortful swallow was used in therapy for 4 months but resulted in nasal redirection that was a consequence of early contact between the base of tongue to posterior pharyngeal wall, blocking the pharynx for bolus transport which caused the bolus to exit through the nose. A VFSS confirmed this observation, and a different strategy was used in therapy according to which the patient was instructed to swallow without effort. After 14 weeks of training on the new non-effortful strategy, nasal redirection was eliminated.

In summary, findings regarding cumulative effects of strength training are contradictory. Studies of persons with dysphagia have reported different results. One case study documented nasal redirection following effortful swallowing (Garcia et al., 2004). Another retrospective study reported on positive results, but the contribution of the high treatment intensity to the results cannot be isolated from the influence of the training approach itself (Huckabee & Cannito, 1999). Similarly, drawing conclusions from the McNeill programme study is also limited (Carnaby-Mann & Crary, 2010). Studies conducted in healthy subjects (Gallas et al., 2009; Macrae, 2011) are also in disagreement. Effortful swallowing is commonly prescribed for patients, but its effects are still not clear, with documentation of both adverse and no-effects in the literature.

3.1.2.1.3 *Contraindication for strength training*

Strength training can lead to adverse effects and is contraindicated in some cases. In healthy individuals, it leads to muscle fatigue, which taxes the muscle and encourages neuromuscular adaptations. Muscle fatigue is a transient, positive event from which the muscle recovers, however, in amyotrophic lateral sclerosis and MS muscle recovery is impeded and fatigue following strength training decreases strength. In addition, applying increase strength in cases of hypertonia can reduce performance, since strength can increase the tone of the muscle even further, thus discomfort and reduction in range of movement, both negative results, will become apparent (Clark, 2003). Also, as reported before, effortful swallowing can lead to negative results (Garcia et al., 2004).

3.1.2.2 Implementation of motor training principles in current swallowing training programmes

As described by Burkhead et al. (2007) and Clark (2003), important motor-training principles underlie adaptations in the neuromuscular system: intensity, specificity, and transference. It is important to remember that even though these are indeed well established in the exercise physiology literature (Savage, 1998), they have yet to be tested for their utility and efficacy in swallowing training. Thus, translation or generalization of these principles into swallowing exercises should take into account differences in muscle composition (Kent, 2004) and control mechanisms (Jean, 2001).

The oropharynx has a unique composition of muscle types as reviewed by Kent (2004). There is a predominance of fast twitch muscles (type II), as well as a unique type of muscle called hybrid fibres which contain more than one type of MyHC isoform, creating combinations like type I + type II fibres (Korfage, Koolstra, Langenbach, & van Eijden, 2005). In addition, there are differences in the characteristics of fibre types. Laryngeal muscles possess type II fibres that have higher contraction speed than those of the limbs (Sciote, Horton, Rowleson, & Link, 2003). In addition, swallowing is mediated mainly by the corticobulbar tract whereas limb movements are controlled by the corticospinal tract. Thus, direct comparison to limb muscles cannot be made without taking these constraints into account (Burkhead et al., 2007; Clark, 2003).

Intensity refers to the load introduced to the muscles, the amount of repetitions, and the duration of training over time. For strength training to trigger muscular adaptations, high intensity exercise must be introduced to push the muscle activity beyond regular use. Thus, if the training goal is to increase strength, introducing increased load levels is critical. The overload principle leads to changes in the ability to generate force, and hence, strength (Burkhead et al., 2007). Training intensity is determined by the training goal: increased force, increased endurance, or increased power (Clark, 2003). In order to increase strength in limb muscles, the initial load, also called physiological load, is 60% of 1RM, where 1-repetition maximum (1RM) is the maximum effort produced in order to complete one repetition. The physiological load is gradually increased during training (Kraemer & Newton, 2000).

In the swallowing literature, the load evaluated in training has been influenced by the skeletal muscle literature. Robbins et al. (2005) found improved force capacity following strength training of a 60% load at the first week followed by 80% load in the remaining 7 weeks. The EMST programme uses the overload principle, similar to that of Robbins et al. (2005), recruiting between 60-80% of the maximum expiratory pressure (Pitts et al., 2009). Shaker et al. (1997)

used the weight of the head as a resistance source and, thus, objective measurements cannot be made. There are no other data to suggest what the most effective load is for swallowing therapy. It might be that a load of 60-80% is indeed the desired load much like in training limb muscles, but no research has compared the effects of different overloads in swallowing training. In the McNeill treatment programme, the authors reported on increasing the size of the bolus, which can be thought of as increased load, in terms of challenge to the motor plan. If the patient had 8/10 successful swallows, a bolus of the higher level in the hierarchy was used, but if the patient showed clinical signs of aspiration in 3 of 5 swallowing attempts, the previous level was used (Carnaby-Mann & Crary, 2008).

In addition to increased load, training dose was found to influence training results. The McNeill programme includes 15 sessions (or less if not needed) of 1 hour each, 5 days a week for 3 weeks and positive results were reported, including increased ability for oral intake (Carnaby-Mann & Crary, 2010). Shaker and colleagues (Shaker et al., 1997; Shaker, Easterling, et al., 2002) found biomechanical changes following 6 weeks of a training programme comprised of 3 repetitions of 1-min sustained head lifts (isometric) and 30 repeated head lifts (isokinetic), 3 times a day, 5 days a week. Pitts et al. (2009) and Troche et al. (2010) found biomechanical changes following 4 weeks of EMST, in which 5 repetitions of effortful breath were performed 5 times a day, 5 days a week. LSVT treatment, which is a voice treatment programme, was performed 1 hour a day, 4 times a week for 4 weeks was shown to have biomechanical effects on swallowing (El Sharkawi et al., 2002). Robbins' group (Robbins et al., 2005; Robbins et al., 2007) found biomechanical and muscular changes following lingual exercise which consisted of 10 (Robbins et al., 2007) or 30 repetitions (Robbins et al., 2005) completed 3 times a day, 3 days a week, for 8 weeks. No research has compared the effects of different intensities in swallowing training on swallowing outcomes. Robbins' group did use different doses, but since the population was different, healthy older subjects (Robbins et al., 2005) and dysphagic (Robbins et al., 2007) individuals, comparisons cannot be made.

Task specificity is an important principle in motor training since functional improvement is shown to be better achieved in a task specific to the training goal (Kleim et al., 2002). If the targeted goal is to improve swallowing function then the training should involve a swallowing exercise that is similar in its characteristics to a 'real' swallowing act. In this regard, the McNeill therapy programme utilizes hard swallowing of a bolus as the training exercise with increased effort. Impairment-focused swallowing exercises performed outside the context of swallowing, like the head-lift exercise (Shaker et al., 1997) or tongue-strengthening exercise using the IOPI (Robbins et al., 2005), do not adhere to this principle. The tongue-hold manoeuvre (Fujiu & Logemann, 1996) and Mendelsohn manoeuvre (Logemann & Kahrilas, 1990) do involve swallowing but alter

swallowing biomechanics by targeting a specific muscle group: forward movement of the posterior pharyngeal wall during tongue-hold, and prolonged UES opening during Mendelsohn's manoeuvre.

Wheeler-Hegland, Rosenbek, & Sapienza (2008) found that the effortful swallowing was a more task-specific technique than EMST or Mendelsohn manoeuvre when measuring the relationship between hyoid movement and submental EMG activity. This indicates that the principle of task specificity is reserved during effortful swallowing. Also, in keeping with the specificity principle, carryover is most likely to occur when the desired behaviour and the practised behaviour are characterized by the same contraction velocity and forces (Clark, 2003). A tongue-exercise study revealed that this principle accounts for the dissociation of its outcomes. Following a month of tongue strengthening, maximum lingual isometric pressure increased, whereas lingual endurance, measured by the ability to produce 50% of the maximum tongue pressure over time, remained unchanged (Lazarus, Logemann, Huang, & Rademaker, 2003). Swallowing requires high velocity contractions during oral transit and pharyngeal phases, thus resembling the characteristics of power training, and requires low forces for relatively longer time periods during the oral processing phase, thus resembling endurance training characteristics. Thus, enhancing endurance and power during swallowing training can theoretically be a desirable goal of swallowing rehabilitation.

According to the *transference principle*, exercise can cause activation of a complex system, including its neural, biomechanical, and muscular components, and therefore can have broad, generalized effects on similar activities or behaviours that were not directly targeted (Burkhead et al., 2007). This principle can account for generalization from the practised task to non-practised but related tasks. More specifically, *transference* can account for the findings regarding the influence of LSVT and EMST training programmes on swallowing (Burkhead et al., 2007) by carrying over effects from the training task (improving voicing and expiratory force, respectively) to the non-training task (swallowing). However, it is important to emphasize that LSVT improved oral-phase dysphagia, and specifically tongue-related function during swallowing, but not pharyngeal phase dysphagia (El Sharkawi et al., 2002). EMST improved volitional cough (Pitts et al., 2009) aspiration/penetration score (Pitts et al., 2009; Troche et al., 2010), and hyoid displacement (Troche et al., 2010), thus improvement via transference was found (Troche et al., 2010).

3.1.3 The need for an alternative approach in swallowing rehabilitation

In physiotherapy, *rehabilitation goals* are determined according to the disorder and its deficits. In swallowing rehabilitation, there are only a few techniques which have been specifically designed to address the underlying physiological deficit; This includes ,head-lift (Shaker, Easterling, et al., 2002) and tongue strengthening (Robbins et al. 2007).

Swallowing disorders are not always a consequence of reduced strength. Delayed pharyngeal swallow and reduced tongue control for example, can also be the underlying impairment. However, there is a lack of specificity in swallowing training and most, if not all, of the current approaches aim to increase strength (Clark, 2003) as discussed earlier. Thus, these approaches can only be used to rehabilitate dysphagia caused by weakness. Weakness is defined as reduced ability to produce force (Clark, 2003), and it can be the result of a variety of insults along the CNS. Weakness can cause a reduction in force, speed of motion, and range of motion (Clark, 2003).

Oropharyngeal muscles can be subjectively assessed for weakness during clinical examination by evaluating the force generated during contraction of the face and mouth against resistant, by observing reduced range of motion, or by assessing coughing or voicing. In addition, swallowing function can be observed using VFFS (Clark, 2003). However, those assessment procedures can only help in *inferring* weakness. Clark, Henson, Barber, Stierwalt, & Sherrill (2003) found that subjective versus objective evaluation of tongue strength were poorly correlated, even among experienced clinicians. Thus, clinical assessment of weakness of the swallowing muscles is subjective and imprecise. The IOPI can offer a precise measure of the tongue pressure and, as was found, increased pressure is associated with increased strength (Robbins et al., 2005), making pressure measurements a proxy measure of strength.

Other than weakness, muscle tone can also be disrupted and affect swallowing (Clark, 2003), but its clinical assessment is difficult. In healthy people, the stretch reflex causes the muscle to contract, as a result of the muscle spindle reaction to passive lengthening or movement. Difficulties in regulating muscle tone can lead to decreased or increased tone (Clark, 2003). Damage to the LMN will affect the efferent component of the reflex and result in hypotonicity, which is clinically difficult to distinguish from weakness (van der Meché & van Gijn, 1986). Damage to the UMN will create interruption to the inhibitory signals and result in hypertonicity. Spasticity and rigidity are forms of hypertonia and can be assessed by voice quality and breath support in speech (Duffy, 1995), but a direct measurement of swallowing hypertonia is difficult to

make, due to inaccessibility of the muscles involved in swallowing and lack of muscle spindles in the lip, tongue and jaw opening muscles (Clark, 2003). Thus, it is hard to apply a passive stretch of the oropharyngeal muscles in order to assess their tone.

Dysphagia can also be caused by incoordination or difficulty executing voluntary motor acts following UMN damage. Patients with PD, for example, exhibit slowness, rigidity and incoordination during swallowing (Aydogdu, Tanriverdi, & Ertekin, 2011). Apraxia of swallowing has also been described after stroke (Daniels, Brailey, & Foundas, 1999; Daniels, 2000; Robbins & Levin, 1988), but there are no objective measures for swallowing incoordination.

Swallowing depends on precision and speed of movement rather than strength (Kent, 2004). Ludlow et al. (2008) discussed the concept of skill training versus strength training in speech. They raised an important point of whether or not strength training is appropriate for actions like speech that are characterized by dynamic fast movements. Following this, a similar question can be raised regarding swallowing. Even in a case of dysphagia due to weakness, will there be transference from training tasks that require force and effort, to the actual functional task of swallowing that require precision and control of executing low levels of force behaviours? (Barlow & Netsell, 1986; Ludlow et al., 2008)

Hamdy et al., (1998) and Clark (2003) proposed that in order for training to effect rehabilitation, it should be chosen based on the pathophysiological basis of the impairment, the observed symptoms and functional needs. Hence, a second question arises in regards to whether approaches that aim to increase muscle strength are appropriate to use for treating dysphagia that is not characterized by weakness. However, with such a striking lack of alternative approaches to swallowing rehabilitation, strength approaches continue to be used.

The paradigm of strength training versus skill training has been investigated in limbs, and the effects of those two types of training have been documented at the muscular and neural level. When compared, skill training has been shown to cause changes at the neurophysiological level, whereas changes due to strength training are at the muscular level (Jensen et al., 2005). However, changes at the neural level following strength training have been documented as well (Griffin & Cafarelli (2007). The possible differentiation in the effects of these approaches is of interest with regards to neurologic dysphagia. It is possible that a skill training approach, whatever that may be, might be more appropriate than strength training, for at least some types of swallowing difficulties.

3.2 Skill training

3.2.1 Skill training of corticospinal skeletal muscles

The mammalian brain has the capacity to alter and adapt function and structure as a result of experience in order to meet specific behavioural demands (Kleim et al., 2002; Nudo, 2006a). The brain's ability to adapt is termed *plasticity*. Plasticity can be driven by sensory stimulation, skill learning, injuries to either the CNS or to the peripheral nervous system, drugs, electrical stimulation, and magnetic stimulation (Nudo, 2006). Of those factors, skill learning is a behavioural procedure, during which the individual is actively participating in learning a new motor skill, and therefore is of interest in the context of rehabilitation. If cortical plasticity can be induced by skill learning in injured nervous systems, rehabilitation should include motor skill learning procedures. To strengthen this point, studies on recovery from induced infarcts in non-human primates, demonstrated that behavioural therapy is a powerful tool leading to recovery (Nudo, 2006).

Evidence from the literature indicates that the cerebral cortex is a malleable, dynamic organ, and plasticity occurs within its structure and thereafter in its function (Kleim et al., 2002). However it is not only the cerebral cortex that demonstrates plastic changes. Functional and behavioural changes have been found in other motor areas, such as the cerebellum (Black, Isaacs, Anderson, Alcantara, & Greenough, 1990; Ito, 2002; Kleim et al., 1998) and BG (Comery, Shah, & Greenough, 1995), that are involved in complex movement execution. Within the cerebral cortex, skill training induces several changes that contribute to improvement in accuracy and speed of performance of skilled behaviour (Guggenmos, Barbay, Bethel-Brown, Nudo, & Stanford, 2009):

1. Increased activation of cortical areas: Increased activation can be the result of expansion or reorganization of cortical representation, due to recruitment of additional motor units during performance of the learnt task (Kelly, Foxe, & Garavan, 2006; Kleim et al., 2002; Nudo & Milliken, 1996). However, increased activation can also be the result of increase in the magnitude of the activated neurons, due to strengthening the neural response of a specific region. Due to low spatial resolution of neuro-imaging techniques, it is difficult to distinguish between those two reasons for increased activation (Kelly et al., 2006).
2. Synaptogenesis: Synaptogenesis is manifested by increased number of synapses per neuron, leading to potential anatomical reorganization. Synaptogenesis can lead to strengthening of intracortical connections between neuronal groups that control the execution of a trained movement (Kleim, Lussnig, Schwarz, Comery, & Greenough, 1996; Kleim et al., 2002).

3. Dendritic branching which is manifested as an increase in the number of branches and increase in the length of the dendrite, and improves the intra-neural communication (Biernaskie, Chernenko, & Corbett, 2004; Withers & Greenough, 1989).
4. Increased expression of brain-derived neurotrophic factor (BDNF) which is a protein that controls neurogenesis (creation of new neurons) (Klintsova, Dickson, Yoshida, & Greenough, 2004).
5. Elevation in c-Fos gene expression which participates in modification of the neuron structure and function (Kleim et al., 1996).

The acquisition of a new motor skill is divided into two stages of learning: an early stage, during which fast improvements in performance occur, and a later stage during which improvement continues but at a slower pace (Karni et al., 1995; Karni & Sagi, 1993). As documented by Kleim et al. (2002) although performance improvement is evident throughout both the early and late stages of learning, neural adaptations occurs only during the late stage of learning, with synaptogenesis taking place first, followed by cortical map reorganization. Since these changes occur in the late stage of learning it is proposed that they represent consolidation of the motor task (Karni et al., 1998; Kleim et al., 2002). It was postulated that during the first stage of learning, topographic transient changes occurred (Classen et al., 1998) and, with increased repetition, these transient neural changes became permanent and were then capable of being observed (Monfils et al., 2005).

LTP and LTD affect synaptic strength and efficacy and are induced during skill learning. LTP and LTD facilitate plasticity following skill training by strengthening intrinsic neural networks or synergies of activation (LTP) and weakening other intracortical connections (LTD). Following skill training in rats, there was an increase in the synaptic strength of horizontal afferent intracortical neurons which connect groups of neurons and together execute the command for motor movement (Riout-Pedotti, Friedman, & Donoghue, 2000). In addition, an increase in LTD and a decrease in LTP was documented (Riout-Pedotti et al., 2000). The same phenomenon was found in Ziemann et al.'s (2004) study on humans, where motor learning enhanced LTD-like plastic changes but prevented LTP-like plasticity. This might be explained by the Bienenstock-Cooper-Munro (BCM) theory, according to which the threshold for inducing LTP/D shifts as a function of previous brain activity (Bienenstock, Cooper, & Munro, 1982). Therefore, the chance of LTD induction increases when LTP has occurred just before (Ziemann et al., 2004). Thus, the documented increase in LTD can be an indirect evidence for earlier-occurring LTP event.

In a study that documented the ability to induce LTP/D mechanisms by paired-stimulation approach, changes were found over the course of a 5-day rapid thumb abduction training (Rosenkranz, Kacar, & Rothwell, 2007). Six young healthy subjects practised for 8 min a day for 5 days. Measurements were taken at baseline, and after the first and the final (5th) training sessions. Motor performance improved significantly over time. Cortical maps changed indicating reorganization following 5 days of training. Induction of LTP-like and LTD-like mechanisms was conducted by using paired-associative stimulation (PAS) to measure plasticity. At baseline, the inhibitory and excitatory paired-pulse protocol resulted as expected: PAS with interstimulus interval of 25 ms facilitated MEP and PAS with interstimulus interval of 10 ms inhibited MEP. After the first training session, the results of the paired-pulse protocol were different to those at baseline, indicating that the first training session was followed by training-induced LTP/D mechanisms. However, the results of the paired-pulse protocols taken after the fifth training session were similar to the ones at baseline, indicating that there were no longer training-induced LTP/D mechanisms. The result of this study are important for the understanding of the processes induced by motor training. LTP/D mechanisms have an important role at the beginning of motor training of a new skill. This mechanism induces strengthening of the synapses and is manifested as improved motor performance. However, over the course of training, the LTP/D mechanisms are reduced and replaced by another process – synaptogenesis. This process involves changes in intracortical neural recruitment and reorganisation of neuronal groups, will be manifested as further improvements in performance, and will be long lasting (Rosenkranz et al., 2007).

Skill learning involves the formation of novel movement sequences and muscle activation patterns. New capabilities of the motor system are acquired during skill learning, as opposed to adaptation of existing motor control mechanisms during strength training (Karni et al., 1998). During practice, the trainee co-activates the same sets of joint movements and muscle contractions, which leads to creation of an activation-module in the motor cortex (Nudo, 2006) resulting in accurate, fast and smooth movement sequences (Hammond, 2002). This activation-module represents the synergistic activation pattern of the new skill. This concept helps in understanding why repetitive movement (Plautz, Milliken, & Nudo, 2000), strength training (Remple et al., 2001), or exercises that do not involve learning of a new motor skill, did not change cortical topography of movement representation. More specifically, the primary motor cortex (M1) is organized in neuronal groups that share the same role and function as a unit. These motor groups react to input in the same manner and give the same output, with each group controlling a discrete movement. Therefore, execution of complex movements involves the coordinated activation of several neuronal groups. Skill learning causes changes in the connectivity between neuronal groups in different regions of the cortex which control the

activation synergy, by strengthening existing synaptic connections of intracortical afferents and by creating new synaptic connections (Adkins et al., 2006; Monfils et al., 2005).

Research by Karni et al. (1995) demonstrated the expression of a learning process at the behavioural and at the neural level, focusing on M1 area using fMRI. A certain movement pattern of the fingers was practised for several weeks at 10-20 min a day. Performance of the trained sequence improved over time, but reached a plateau at 3 weeks. At the same time, an M1 activation map that was evoked during performance displayed expansion of neural representation, in comparison to the activation evoked during the untrained sequence. This enlargement was consistently detected in comparison to the untrained sequence weeks after the training was discontinued (Karni et al., 1995) with no deterioration in performance up to 1 year after training was discontinued (Karni et al., 1998).

Pascual-Leone et al. (1995) used TMS to compare the cortical motor area and activation threshold of M1 hand area between two groups: a skill-training group who practised a right-hand five-finger exercise on the piano, and a control group who played the piano using only the right hand but were not taught the five-finger exercise. Both groups trained for 5 days, 2 hours per day. Cortical motor outputs of the controls were substantially less prominent than those in the skill learning group.

Jensen et al. divided a group of 24 healthy young participants (20-30 years old) into 2 groups. The strength-training group performed heavy load strength training of the dominant right arm elbow flexors as reported earlier in this chapter. The skill-training group also performed motor training of the right arm elbow flexors, but they were required to precisely perform different series of combinations of flexion and extension movements shown on a screen. Both groups completed 13 training sessions over 4 weeks. The skill-training group demonstrated greater corticospinal excitability, even after 2 weeks of training, and their performance was improved. The strength training group had increased muscle strength in the presence of decreased MEP magnitude, as discussed before (Jensen et al., 2005).

3.2.1.1 Plastic changes following cerebral injury in the limb motor areas

Following brain injury plastic changes occur, even without intervention (Nudo, 2006b). Spontaneous neural recovery occurs within the damaged area (Nudo, 2003). In addition, compensatory plastic changes occur at the neural substrate that lays close to the injured tissue in the ipsilateral hemisphere, and also in the contralateral hemisphere (Nudo, 2006b). New

connection between brain areas are formed to allow intact brain areas to contribute to recovery (Nudo, 2006b, 2007).

Nudo & Milliken (1996) showed that 1 hour per day of skill training following induced cerebral infarcts prevented the loss of hand area representation in cortical areas close to the lesion. When intervention was not given, this representation was lost. In addition, the training caused an expansion of the hand area to areas that were representing other movements before the induced infarct. Liepert, Graef, Uhde, Leidner, & Weiller (2000) demonstrated that one hour of training aimed to improve hand dexterity in stroke patients with hemiparesis resulted in improved function and increased MEP magnitude immediately after training and also at one day post-training. Constraint induced movement therapy can also be considered as skill training treatment, since the use of the affected extremity is heavily increased during functional tasks, whereas the healthy extremity is not used. Following 12 days of constraint induced treatment in 13 chronic stroke patients, the representational map of the affected hemisphere enlarged as found in a TMS study, and this extension was a result of recruitment of adjacent areas. Six months following training, the size of the affected and intact hand brain areas were similar, resembling the balance found in healthy subjects, and motor performance remained high (Liepert, Bauder, et al., 2000).

A recent study by Boyd, Vidoni, & Wessel (2010) compared sequence-specific skill training to a non-specific increased use of the paretic arm, in 18 chronic unilateral middle cerebral artery stroke patients. Functional MRI scans were performed pre-training and 1 day post-training. The patients trained for 3 days, with both training groups performing the same amount of arm movements. The skill group demonstrated a decrease in the neural activity in the contra-lesional (i.e., ipsilateral) hemisphere, reflecting a return to a normal activation pattern, in which the contralateral hemisphere to the arm is activated, rather than the ipsilateral hemisphere. The other group that performed non-specific arm training did not demonstrate these changes (Boyd et al., 2010). These studies reflect the beneficial contribution of skill training, whether it is in the form of constraint induced training that encourages functional arm use or specific skill learning, on motor and neural recovery following stroke.

3.2.2 Skill training in swallowing

The influence of swallowing training, and more specifically of skill training, on swallowing has not been investigated at the neural level. However, the effects of specific oral motor training at the neural level have been documented.

Studies have documented the effects of a tongue protrusion task on cortical excitability and reorganization in primates (Sessle et al., 2007; Sessle et al., 2005) and humans (Arima et al.,

2011; Boudreau et al., 2007; Svensson et al., 2003, 2006). Sessle et al. (2005; 2007) trained monkeys for a month and measured the response from the task related facial cortical area and from the masticatory area not directly related to the training task, in order to document carryover. They found that the area from which tongue protrusion was evoked by intracortical microstimulation expanded, and more neurons were related to tongue protrusion upon stimulation; however, the cortical area for eliciting lateral tongue movement had decreased in size. The cortical areas for mastication did not show any changes. These findings emphasize the importance of using task specific training to generate neural adaptation.

Svensson et al. (2003) used TMS to examine the effects of the same novel tongue protrusion training task on cortical excitability in 11 young healthy participants. They performed the task for 7 consecutive days, 60 min a day. MEPs from M1 were collected at baseline, 30 min following the final training session and two weeks after that. During the 7 days of training, performance gradually improved while a gradual decrease in self-reported fatigue occurred. MEPs increased in amplitude post-training; however, at two weeks post-training the MEP amplitude was similar to that at baseline. In addition, the tongue cortical motor maps expanded post-training in comparison to baseline. Later, two studies examined the influence of 1 hour of tongue training, using TMS (Svensson et al., 2006) and fMRI (Arima et al., 2011) as assessment tools. Neurophysiological excitability was measured 30–60 min post-training and at 1 day and 7 days post-training. The TMS study results revealed lower motor threshold at post-training and at 1 and 7 day follow-ups, and a larger motor map area at 1-day follow-up compared to baseline and 7 days post-training (Svensson et al., 2006). The fMRI study documented changes in brain activity at all time points, including 1 week post-training, although different brain regions showed different activation patterns along that time course (Arima et al., 2011). Svensson et al. (2006) concluded that M1 is likely to exhibit plasticity that mediates, to some extent, the acquisition of orofacial motor tasks, and that the face area of M1 is highly adaptive in response to new motor tasks. This dynamic reaction may play a role in learning complex tasks related to swallowing, like bolus preparation during the oral stage. However, the studies discussed above measured only neurophysiological changes. It is still not clear whether tongue protrusion exercise can affect swallowing biomechanics, like tongue pressure against the palate during swallowing, or base-of-tongue pressure against the posterior pharyngeal wall. Documenting measurable neurophysiological changes is an important step towards measuring exercise effects but, by itself, it is not enough, since neural changes might not translate into biomechanical changes. In addition, biomechanical changes seen following oral motor training exercises in healthy primates (Sessle et al., 2007; Sessle et al., 2005) or humans (Arima et al., 2011; Boudreau et al., 2007; Svensson et al., 2003, 2006) might not translate into functional changes in patients with dysphagia.

To summarize, the current literature suggests that corticobulbar skill training can cause changes at the neural level. The specificity of the task is important as limited functional carry-over was documented in healthy subjects and stroke patients. The possibility that swallowing-related skill training can create enduring changes at the neural level is intriguing for rehabilitation of neurogenic dysphagia.

3.3 Biofeedback and motor learning

3.3.1 Biofeedback

During the process of motor learning, a motor plan is shaped and refined through a process of feedback (Rose & Robert, 2006; Schmidt & Lee, 1999). Feedback can be available through two sources: an internal source and an external (augmented) source. Both types of feedback enhance motor learning. During performance, sensory information from joint receptors, muscles spindles, and golgi tendons organs is registered by sensory receptors, and this kinesthetic intrinsic feedback is transferred to the CNS. An evaluation of movement accuracy is made, and if a mismatch between the plan and the actual performance occurs, a correction process takes place. This represents an internal feedback process.

When provided externally, the feedback is said to be ‘augmentative’ as it enhances the already existing internal feedback. Augmented feedback can be delivered in three forms. Knowledge of results feedback provides information about the outcome of the motor act (e.g., the score, correct or incorrect). Knowledge of performance feedback provides information about the movement itself (e.g., you have bent your elbow to a 90 degree angle). Lastly, augmented feedback can be delivered by biofeedback in which the sensory intrinsic feedback that is related to the motor or physiological event is enhanced (Rose & Robert, 2006). Biofeedback involves measuring physiological events and displaying those in real time. This allows the subject to manipulate those physiological events to gain increased control (Basmajian, 1989).

3.3.2 Biofeedback and dysphagia

Biofeedback has been used in dysphagia treatment as an adjunctive treatment tool to increase awareness of the swallowing process and to increase the patient's control over performance, by offering concrete external monitoring that allows improvement of disordered swallowing. In addition, biofeedback has also been used to monitor correct performance of swallowing manoeuvres and to assess correct implementation of swallowing exercises (Barofsky, 1995; Burkhead et al., 2007)

Surface EMG is one of the modalities used as a biofeedback tool for measuring muscle activity, and its use in dysphagia rehabilitation is supported by several studies. A retrospective study by Huckabee & Cannito (1999) reviewed the outcomes of intensive treatment that included traditional training augmented by sEMG biofeedback, as discussed earlier in this chapter. Their data provided support intensive treatment with biofeedback. Crary et al. (2004) supported the use of biofeedback to improve outcomes in chronically-impaired patients as a result of stroke and head and neck cancer. Biofeedback was used to teach the patients the Mendelsohn manoeuvre, which requires increased motor control (Crary, Carnaby-Mann, Groher, & Helseth, 2004). It is impossible to attribute the positive changes reported to the use of biofeedback, since other factors were not controlled, such as treatment intensity, patient population, and motivation. Reddy et al. (2000) utilized dynamic acceleration biofeedback to augment the performance of various swallowing manoeuvres and documented improvement in swallowing as assessed by VFSS in patients with dysphagia due to various aetiology following nine treatment sessions (Reddy et al., 2000). However, the study design is weak, being based on only five case reports of dysphagic patients with different aetiology. Although each patient received nine treatments, the frequency differed, ranging 1–3 times per week. As mentioned before, a more recent study (Carnaby-Mann & Crary, 2010) compared a traditional approach to swallowing rehabilitation, that utilized swallowing manoeuvres accompanied by sEMG biofeedback, to McNeill therapy, which is characterized by a structured and intense format, without the use of biofeedback. This study is characterized by several confounding factors, as described earlier, and therefore although the authors claim that the McNeill programme is superior to traditional treatment with biofeedback, their study is insufficient to indicate that biofeedback as an adjunct tool is not beneficial.

To summarize, biofeedback is a common tool in swallowing rehabilitation that provides the trainees with conscious ‘access’ to muscles that do not provide sufficient sensory information, partly due to lack in muscle spindles and joint receptors (Clark, 2003; Kent, 2004). Evidence for its effectiveness in swallowing rehabilitation is still lacking. Previous studies utilized immediate and ongoing feedback in treatment protocols. However, there is evidence to suggest that other feedback protocols, like delayed feedback, may facilitate greater gains for motor learning (Salmoni, Schmidt, & Walter, 1984; Schmidt & Lee, 1999).

3.3.3 Timing of feedback – Immediate versus delayed

Timing of feedback has been found to be important in motor learning. The time interval between the performance and the feedback presentation is referred to as the *feedback delay interval*. When feedback is given throughout the performance in an online fashion, it allows the trainee to correct the performance in real time. This is termed immediate feedback. Delayed feedback is given after

the performance, and thus does not allow the trainee to correct the physiological behaviour, but allows examination of its results.

According to the guidance theory (Salmoni et al., 1984; Schmidt & Lee, 1999), when feedback is given too frequently, it can lead to over-dependence on the external feedback leading to deterioration of task performance when the feedback is not present (Proteau, Marteniuk, & Lévesque, 1992). In addition, immediate or frequent feedback does not allow enough time for engaging in cognitive processes that are important for developing internal error-detection and correction capacities, and also prevents processing of internal intrinsic sensory information (Salmoni et al., 1984). The effects of delayed feedback have been studied in relation to limb movements and in the area of speech disorders. Swinnen, Schmidt, Nicholson, & Shapiro (1990) found that an 8-s delayed feedback on a hand movement task resulted in better performances on a retention task than immediate feedback. In the area of speech rehabilitation, a qualitative study of 2 patients with apraxia of speech showed that a 5-s delayed feedback manifested in better retention scores whereas immediate feedback resulted in better acquisition scores (Hula, Austermann, Robin, Maas, Ballard, & Schmidt, 2008). This is supported by other existing literature (Bruechert, Lai, & Shea, 2003; Salmoni et al., 1984). There are no reports in the literature regarding the use of a delayed feedback protocol for swallowing. However, based on the theoretical frame and research findings in other domains, delayed feedback might be also prove beneficial for improving control of swallowing.

CHAPTER 4:

AIMS AND HYPOTHESES

4.1 Aims

This research project represents the first step for exploring the effects of swallowing skill training, and includes two Phase I clinical-trial studies.

The main aim of this study was to fulfil the requirements of Phase I clinical research, which include assessment of training safety, assessment of training protocols, selection of the most sensitive outcome measures following training, estimation of training dosage, and measurement of the magnitude of changes. This aim follows on the recommendation of Robey & Schultz (1998), Robey (2004a), and Whyte et al. (2009).

The secondary aim of the study was to explore differences between training. Since skill training was developed as an alternative to effortful swallowing, it was important to assess if indeed difference were indicated. Effortful swallowing was chosen as the ‘contrast’ approach to skill training as it is different from skill training in only one dimension. Both training approaches include swallowing execution, thus both have a ‘skill’ component. However skill training emphasises increased precision in swallowing whereas effortful swallowing emphasises increased strength in swallowing. This one-dimensional difference can help clarify the source of differences, if any, between the two training approaches. Hypotheses were formed to explore data in the main study ‘Skill versus strength in swallowing training in healthy subjects’ and the pilot study ‘Effects of increased dosage of training sessions’ are presented below.

A two-week training period was chosen based on a study by Huckabee & Cannito (1999) of a two-week intensive swallowing rehabilitation programme utilizing biofeedback, which resulted in positive results in post-stroke patients with dysphagia, and also based on a study by Jensen et al. (2005) that documented neural adaptations in healthy subjects after 2 weeks of limb training. In addition, a pilot study consisting of additional training sessions was conducted in order to establish the optimal dose for intervention, as suggested by Dobkin (2005).

Effortful swallowing is a widely-used approach in swallowing rehabilitation (Lazarus, Logemann, Song, Rademaker, & Kahrilas, 2002). It is widely investigated in the literature (Wheeler-Hegland et al., 2009), although mostly for its immediate effects, with some literature documenting its

cumulative effects (see Chapter 3). The novel approach of swallowing skill training was compared to a traditional approach consisting on effortful swallowing in this current study. Traditional approaches, including effortful swallowing and other strength training approaches, have previously been used as a ‘control’ task, to which other (new) approaches are compared. For example, Wheeler-Hegland, Rosenbek, & Sapienza (2008) compared the immediate effects of a new training approach of EMST to effortful swallowing. Logemann et al. (2009) compared the cumulative effects of head-lift training to a ‘traditional’ training that included Mendelsohn manoeuvre and tongue-base strengthening among people with dysphagia.

In the current study, skill training was subdivided into two groups with different feedback schedules: one offering immediate visual feedback and one offering delayed visual feedback. This was done to assess the differences in the effects of the two training protocol, and ultimately to identify which has superior effects.

Differences between the two training approaches – skill and strength training – were expected to occur at three levels: neurophysiological, biomechanical, and structural. Hypotheses are suggested for each of these levels. In addition, since a new training approach of skill training and new training protocols were utilized, hypotheses are presented regarding the motor performance and the subjective ratings of each training protocol.

The hypotheses presented below are for the main study and the pilot that consist of additional training sessions. It is hypothesized that the same trends detected following the 2-week training protocol would further change (in the same direction) following the additional training sessions.

4.2 Hypotheses regarding neurophysiological changes

4.2.1 The effects of skill training versus strength training on

MEP area

Unresolved questions

Is there a difference in the immediate changes following training in submental MEPs area between skill training and strength training, in healthy subjects?

Is there a difference between skill training and strength training, in healthy subjects in the immediate changes that occur at the beginning of the training in comparison to the immediate changes that occur at the end of the training?

Is there a difference in the cumulative effects of training in submental MEPs area between skill training and strength training, in healthy subjects?

Hypotheses

- H1) Strength training in comparison to skill training will result in greater changes in MEP area recorded during effortful submental muscle contraction, immediately after training.
- H2) Skill training in comparison to strength training will result in greater changes in MEP area recorded during volitional saliva swallowing, immediately after training.
- H3) Skill training will result in a decreased magnitude of swallowing-related MEPs recorded immediately after the last training session, in comparison to strength training. Strength training will result in a decreased magnitude of contraction-related MEPs recorded immediately after the last training session, in comparison to skill training.
- H4) Strength training in comparison to skill training will result in a greater increase in MEP area recorded during effortful submental muscle contraction, following the complete training period.
- H5) Skill training in comparison to strength training will result in a greater increase in MEP area recorded during volitional saliva swallowing, following the complete training period.

Rationale

Griffin & Cafarelli (2007) found that 2 weeks of resistance training composed of maximal volitional contraction of the lower limb, resulted in increased MEP amplitude recorded during the same task as the training task (i.e., muscle contraction). This increase in excitability would reflect the results of ‘strength learning’ process (Griffin & Cafarelli, 2007) by which execution of force can become more efficient and coordinated by changing recruitment patterns of type I and II motor units (Burkhead et al., 2007; Clark, 2003). Similarly, the current study holds the hypothesis of increased MEP magnitude following strength training.

Skill training has not been explored in the area of swallowing training. Evidence from the literature suggests that skill training of limb movement can result in increased MEP magnitude following 2 weeks and 4 weeks of training (Jensen et al., 2005). In contrast, an fMRI study found that 3 days of skill training of the arm muscles among stroke patients with hemiparesis, resulted in a decrease in brain activation in the ipsilateral hemisphere which reflected physiologic recovery and a return to unimpaired activation (Boyd et al., 2010). Thus, skill training would result in improved function either by increasing excitability or reducing an unnecessary activation.

Neural adaptation occurs in early stages of strength training (Folland & Williams, 2007; Komi, 1986) and lasts throughout later stages of strength training (Burkhead et al., 2007; Moritani, 1993). Skill training is also characterized by early occurrence of neural changes (Karni et al., 1995). Thus, for both trainings, changes in MEP magnitude are hypothesised to appear immediately after one training session and to continue to appear immediately after 10th and 18th training sessions. In addition, cumulative effects of training can result in neural adaptations that would be measurable following the whole 2 weeks and 4 weeks training period.

LTP/LTD take place immediately after motor learning (Rioul-Pedotti et al., 2000; Rosenkranz et al., 2007; Ziemann et al., 2004) and last for approximately 2 hours (Ziemann et al., 2004) during which strengthening/weakening of synaptic transmission occurs (Thompson et al., 2005). MEP magnitude reflects the activation/depression mode of the neural networks (Ziemann et al., 2004). Following training, changes in neural adaptations, as a consequence of synaptic strengthening or weakening, are expected to be present. Since the different training approaches introduce different types of learning (force execution vs. precision of movement) differences in LTP/LTD mechanisms related to the training type are expected to be present when measured immediately after training. These immediate changes in LTP/LTD will decrease as the training proceeds, reflecting consolidation of the behaviour over time (Rosenkranz et al., 2007) .

Although strength training employs swallowing execution, the main emphasis of this technique is to increase muscle contraction force. Hence, strength training, but not skill training, will influence MEP magnitude recorded during effortful contraction. By the same token, since skill training employs mainly non-effortful saliva swallowing, skill training, but not strength training will influence MEP magnitude recorded during non-effortful saliva swallowing. The basis for these hypotheses also emerges from the literature regarding principles of motor learning (see *Chapter 2 - Literature Review*). Carryover effects are likely to occur when the desired behaviour and the practised behaviour are characterized by the same contraction velocity and forces (Clark, 2003). More specifically, since skill training employs saliva swallowing, there will be a carryover to the swallowing task during MEP data collection. Since strength training employs effortful swallowing which is characterized by prolonged duration (Wheeler-Hegland et al., 2008), there will be carryover to the contraction task.

Significance

It is not clear whether an increase or a decrease of submental MEPs amplitude following swallowing training is a positive or a negative outcome. Greater MEPs magnitude can indicate lower recruitment threshold of the motor units (Griffin & Cafarelli, 2007). It can also indicate improved coordination and creation or re-enforcement of existing synergies of activation

(Burkhead et al., 2007; Clark, 2003), or improvement in the efficiency of motor unit recruitment patterns controlled by the CNS (Barlow, 1999). However, greater MEP magnitude can also represent decreased activation of inhibitory control circuit (Peinemann et al., 2001). Thus, it is important to clarify the direction of neural change among healthy subjects first, before assessing the effects of training approaches on the dysphagic population.

Strength training is often prescribed for patients with swallowing difficulties. However, its influence on functional swallowing, which is a sub-maximal activity, is not clear. Skill training, which represents a more functional task than submental muscle contraction, is expected to have greater influence than strength training on MEP amplitude during volitional saliva swallowing.

The presence of immediate changes in MEP magnitude following the training session can indicate whether providing swallowing training prior to mealtime can increase neural activation during the meal itself, and potentially improve swallowing function. Providing multiple training sessions is expected to affect the LTP/LTD mechanisms that occur immediately following training.

Neural adaptations or plastic changes are of importance for recovery in general (Nudo, 2007), and for swallowing rehabilitation in particular. Dysphagia is a prevalent symptom following several neurological conditions, such as stroke, TBI, PD, etc. (Perlman & Schulze-Delrieu, 1996). Changes to the neural substrate as a consequence of training might alleviate the symptoms among such dysphagic patients. Lack of influence can indicate that a specific training approach or protocol of administration may not be an appropriate treatment option.

Proposed studies

1. MEPs will be recorded in healthy subjects during submental muscle contraction and during volitional swallowing of saliva at 5, 30, 60 and 90 min post training immediately following the first training session, and the 10th training session and, in a subgroup of this cohort, after the 18th training session (see Chapter 6).
2. MEPs will be recorded in healthy subjects during submental muscle contraction and during volitional swallowing of saliva before and after 2-weeks of swallowing training, and in a subgroup of this cohort, after 4-weeks of swallowing training (see Chapter 6).

4.3 Hypotheses regarding biomechanical changes

4.3.1 *The effects of skill training versus strength training on pharyngeal and UES pressure events*

Unresolved question

Is there a difference between skill training and strength training on pharyngeal and UES peak pressures and durations as measured by pharyngeal manometry in healthy subjects?

Hypotheses

- H6) Strength training in comparison to skill training will result in a greater increase in pharyngeal (upper and mid-pharynx) peak pressure and duration, a higher UES nadir pressure (i.e., less negative pressure), shorter duration of UES opening, and a shorter time interval between the occurrence of the pressure events at the pharynx and UES (i.e., relative timing representing the sequencing of the pressure events), during the effortful saliva swallowing task, which will transfer to effortful bolus swallowing.
- H7) Skill training in comparison to strength training will result in a greater increase in pharyngeal (upper and mid-pharynx) peak pressure and duration, greater decrease in UES nadir pressure (i.e., more negative pressure), and longer duration of UES opening, in the non-effortful saliva swallowing task which will carry over to non-effortful bolus swallowing.

Rationale

Although the cumulative effects of effortful swallowing on biomechanical events have not been documented, there is evidence in the literature regarding the immediate effects of task execution. These findings indicate that effortful swallowing can result in increased pharyngeal pressure and duration (Huckabee et al., 2005). In addition, a decrease in UES nadir pressure (Huckabee et al., 2005) and increased UES opening duration (Hind et al., 2001) have been documented during the execution of effortful swallowing. However, it is possible that the decreased anterior hyoid movement documented in healthy subjects during effortful swallowing (Bülow et al., 1999; Hind et al., 2001) will affect UES opening, with reduced UES pressure and shorter duration due to cumulative effects of training. No study had measured the short-term or cumulative effects of effortful swallowing on the *relative timings* of the pressure events (i.e., sequencing of the pharyngeal pressure events occurrence at different areas of the pharynx and the UES), but one

study reported a potential adverse effect of cumulative effects of this exercise, which was characterized by reduced time interval between pharyngeal pressure events (Garcia et al., 2004). In addition, Bulow et al. (2001) reported reduced pharyngeal clearance when executing effortful swallowing (Bulow et al., 2001).

Swallowing skill training has not been previously investigated. However, reports on the effects of skill training in limbs indicates that no change in force generation during maximal contraction, although increased accuracy was present (Jensen et al., 2005). Thus, by inference, increased precision of pharyngeal events are expected to be expressed by increased pressure and duration of the pharyngeal pressure events in non-effortful (i.e., functional) swallowing, consequently resulting in improved pharyngeal clearance (Pauloski et al., 2009). In addition, transference from the practised task to a similar task that involves swallowing of a water bolus may follow (Burkhead et al., 2007).

Significance

When first introduced, effortful swallowing was recommended as a swallowing manoeuvre to increase pressure and improve bolus propulsion and clearance through the pharynx (Kahrilas et al., 1991, 1992; Logemann & Kahrilas, 1990). However, it was later prescribed to patients with dysphagia as a rehabilitation exercise (Crary, 1995; Huckabee & Cannito, 1999). Despite this, there is sparse evidence for the cumulative effects of this manoeuvre on swallowing biomechanics, including pharyngeal and UES pressures. In addition, there is a report of potential adverse effects (Garcia et al., 2004) that might be related to disproportional increase in pressure or distorted timing of the pressure events. Hence, it is important to document the cumulative effects of this exercise on pharyngeal and UES pressure events (peak pressure and duration, and their timing). Skill training, as opposed to strength training, is offered as an alternative to effortful swallowing in dysphagia treatment, for cases in which weakness is not the cause of dysphagia. Skill training will have a greater influence than strength training on pharyngeal and UES pressure events during volitional non-effortful saliva and water swallowing, which represents a more functional task than effortful swallowing. Additionally, increased pharyngeal clearance and increased precision of pharyngeal events would lead to a more efficient swallowing that will result in less pharyngeal residue and reduced risk for aspiration post swallowing. Lastly, in Phase I clinical outcomes research, it is important to assess intervention safety; i.e., rule out the occurrence of adverse affects.

Proposed study

Pharyngeal pressure will be measured in healthy subjects before training and after 2 weeks of training using pharyngeal manometry. In a subgroup of the original cohort, pressures will be evaluated again after 4 weeks of swallowing training. Pressure will be measured at two levels of the pharynx: the upper pharynx, where the posterior tongue contacts the posterior pharyngeal wall, and the mid-pharynx, at the level of the laryngeal additus. In addition, a pressure sensor will be located at the level of the UES. Four types of tasks will be evaluated: non-effortful swallowing tasks of saliva and 10 mL water, and effortful swallowing tasks of saliva and 10 mL water (see Chapter 6).

4.3.2 The cumulative effects of skill training versus strength training on submental sEMG

Unresolved question

Is there a difference between skill training and strength training in submental muscle activity as measured by sEMG in healthy subjects?

Hypothesis

- H8) Strength training in comparison to skill training will result in a greater increased sEMG peak amplitude recorded from the submental muscles during effortful swallowing tasks (effortful saliva swallowing and water swallowing) but not in non-effortful tasks (saliva swallowing and water swallowing).
- H9) Skill training in comparison to strength training will result in a greater increased sEMG peak amplitude recorded from the submental muscles during non-effortful swallowing tasks (saliva swallowing and water swallowing) but not in effortful swallowing tasks (saliva swallowing and water swallowing).

Rationale

Strength training of muscles of the limbs resulted in increased muscle force in comparison to skill training (Jensen et al., 2005). Thus, it is expected that strength training of the submental muscles will result in increased sEMG peak amplitude during effortful tasks. In contrast, skill training will result in an increase in sEMG peak amplitude in non-effortful tasks, which may indirectly reflect more efficient firing patterns for the trained task (non-effortful swallowing of saliva) according to the task specificity principle (Barnett, Ross, Schmidt, & Todd, 1973) that states that performance

will improve if the training consist of the activity itself (Ranganathan & Newell, 2010; Rushall & Pyke, 1990). Carryover is expected to occur from the practice task to a bolus (non-effortful 10 mL water) swallowing task (Burkhead et al., 2007).

Significance

An increase in the submental sEMG peak amplitude would indicate that strength training of the submental muscles results in an increase in force. Increased force might be related to hypertrophy of the muscles. Increased force might also relate to improved neural drive, including coordinated firing patterns of motor neurons, increased recruitment of motor neurons, or recruitment of bigger motor units. In addition, an increase in muscle activation in non-effortful tasks following skill training would indirectly reflect a more efficient control over the muscles in functional swallowing tasks. Examining the results of this investigation, in light of results from other outcome measures, will help to distinguish between muscular and neural sources of change.

Proposed studies

Peak amplitude of submental sEMG will be measured in healthy subjects before training, after 2 weeks of training, and, in a subgroup of the cohort, after 4 weeks of training. Four types of tasks will be evaluated: saliva swallowing and 10 mL water swallowing (non effortful tasks) and effortful saliva swallowing and 10 mL water swallowing (effortful tasks).

4.3.3 The effects of skill training versus strength training on hyoid displacement

Unresolved question

Is there a difference between skill training and strength training on hyoid displacement as measured by ultrasonography in healthy subjects?

Hypothesis

H10) Strength training in comparison to skill training will result in a reduction of hyoid displacement during swallowing.

Rational

There are conflicting results regarding the immediate effects of effortful swallowing on hyoid displacement, with both decreased displacement (Bülow et al., 1999) and no effect (Wheeler-Hegland et al., 2008) reported in the literature. Cumulative effects of effortful swallowing can

potentially strengthen the submental muscle group and, hence, increase anterior pull over the hyoid (Pearson, Langmore, Yu, & Zumwalt, 2012). However, since effortful swallowing in a non-specific exercise for submental strengthening (Logemann, 1988; McConnel, 1988) repetitive performance of effortful swallowing may have cumulative effects on the pharyngeal musculature. Strengthening the pharyngeal constrictors may lead to an antagonistic backward force on the hyoid bone during swallowing and, hence, restrict hyoid displacement.

Significance

Although it is prescribed to patients with dysphagia as a rehabilitation exercise (Crary, 1995; Huckabee & Cannito, 1999), the cumulative effects of effortful swallowing on hyoid displacement have not been documented. The hyoid plays an important role in swallowing; thus, it is imperative to investigate potential negative effects of decreased hyoid displacement.

Proposed study

Hyoid displacement will be measured using ultrasound before training and after 2-week training, and, in a small group, 4-week training. The percentage of change from hyoid rest position to its maximum displacement will be calculated (see Chapter 6).

4.4 Hypothesis regarding structural changes

4.4.1 The effects of skill training versus strength training on the cross sectional area of the submental muscles

Unresolved question

Is there a difference between skill training and strength training on changes to the CSA of the anterior belly of digastric and geniohyoid muscles in healthy subjects?

Hypothesis

H11) Strength training in comparison to skill training will result in a greater increase in the CSA of the digastric and geniohyoid muscles.

Rational

Strength training results in morphological adaptations of the muscles leading to muscle hypertrophy (Folland & Williams, 2007). Specific to swallowing, previous research (Robbins et

al., 2005) identified an increase in the tongue CSA following strength training of the tongue muscles. Thus, it is presumed that strength training focused on the submental muscles will result in an increase in the CSA of the anterior digastric and geniohyoid. Skill training of hand muscles, on the other hand, did not result in increase muscle force (Jensen et al., 2005), hence it is likely that hypertrophic changes will not be present following swallowing skill training.

Significance

An increase in the CSA of the submental muscles will indicate that strength training of the submental muscles can result in increased force due to hypertrophy.

Proposed study

The CSA of anterior belly of right and left anterior belly of digastric and geniohyoid muscles will be measured before training and after 2 weeks of training, and in a smaller group, after 4 weeks of training (see Chapter 6).

4.5 Hypotheses regarding participant's performance

4.5.1 Participants' performance during training: the effects of strength training on submental EMG

Unresolved questions

Does swallowing strength training result in increased submental sEMG activity in healthy subjects?

Hypothesis

H12) Swallowing strength training will result in a gradual increase in submental muscle activity over the course of training, as measured by the averaged sEMG peak amplitude collected during each of the training sessions.

Rationale

Strength training of limb muscles resulted in increase muscle force (Jensen et al., 2005). Thus, it is expected that strength training of the submental muscles will result in a gradual increase of peak amplitude over the course of the training period.

Significance

Achievement of training goals - increased strength during the course of strength training - can assist in interpretation of the other outcome measures. If the subjects did achieve the training goal, then the other outcome measures can be evaluated in light of fulfilment of the training goal. However, if the goal was not achieved, then the lack of changes following training may be related to poor task execution. In addition, not achieving the goals can identify a need for designing a better/different protocol for training.

Proposed study

Submental muscle activity will be recorded throughout the training sessions in the 2-week and 4-week training protocols for subjects in the strength training (see Chapter 6).

4.5.2 Participants' performance during training: evaluation of the skill training protocol

Unresolved question

Is there a difference in the changes in motor performance (target hit-rate) during training between swallowing skill training with delayed visual feedback and skill training with immediate visual feedback in healthy subjects?

Hypothesis

H13) Skill training with immediate feedback will result in a greater change in performance during training (i.e., the difference in hit-rate over time will be reduced) than skill training with delayed feedback.

Rationale

Learning a new task involves creating a motor plan. Both skill training protocols (delayed and immediate feedback) employ the use of visual biofeedback to promote learning. Over the course of training, increase in performance accuracy will be exhibited during both training protocols. However, using delayed feedback during the process of motor learning will create a harder task that will introduce an increased demand for planning the motor movement and concentration, in comparison to immediate feedback. During this process, the trainee in the delayed feedback protocol is required to internalize the sensory information and to develop internal mechanisms of error detection and correction, since external feedback is missing. Eventually subjects completing

skill training with delayed visual feedback will gain more control and better accuracy since they rely on internal clues rather than external ones. However, during the process of learning, subjects in the delayed feedback protocol will have poorer motor performances due to greater task difficulty than subjects in the immediate feedback protocol (Rose & Robert, 2006).

Significance

Delayed feedback can be beneficial for improving control over swallowing as it requires increased planning, concentration and internalization of proprioceptive information (Rose & Robert, 2006) involved in swallowing execution.

Proposed study

Hit rates of the training target will be recorded during the training sessions in the 2-week and 4-week training protocols for skill training subgroups: skill with immediate feedback and skill with delayed feedback (see Chapter 6).

4.6 Hypothesis regarding subjective ratings of the training

4.6.1 Participant's subjective ratings of the swallowing training

Unresolved question

Is there a difference between skill training and strength training in participant ratings of the training task in healthy subjects?

Hypothesis

H14) Skill training will exhibit more positive participant subjective ratings than strength training.

Rational

Previous research has documented positive acceptance and high compliance of patients to biofeedback assisted treatment (Kuiken, Amir, & Scheidt, 2004). The current study employs the use of interactive computer software that provides visual biofeedback. Since skill training offers more varied and practice in comparison to strength training, which is, in essence, repetition of effortful swallowing, skill training group members will rate skill training in a more positive way.

Significance

Participant's ratings of the training in terms of enjoyment, boredom, or complaints about pain can be used to refine training protocol.

Proposed study

Questionnaires will be given to the members of the strength-training group and skill training groups following completion of 2-week training and, in a smaller group, 4-week training (see Chapter 6).

CHAPTER 5: ASSESSMENT AND TRAINING METHODS

5.1 Participants

Forty two healthy adult participants were recruited. Two did not complete the study (see 5.1.1). The remaining 40 participants equally represented and matched for gender and age group (young: mean \pm SD = 25.25 \pm 4.07, range 21-35; old: mean \pm SD: 68.75 \pm 9.55, range 53-88) were evenly divided into two training groups: skill training (SKL) and strength training (STR). The two groups were matched for gender and age (Table 5.1). The SKL group was further subdivided into two equal subgroups: skill training with immediate visual feedback (SKL-I) and skill training with delayed visual feedback (SKL-D) (Table 5.2).

Table 5.1 Ages (in years, mean \pm SD, range in brackets) of the skill (n=20) and strength (n=20) groups

Age group	Gender	SKL	STR
Young (n=20)	Female (n=10)	23.83 \pm 3.18 (21-30)	27.4 \pm 6.1 (22-35)
	Male (n=10)	25.75 \pm 4.42(21-30)	24.4 \pm 2.07(22-27)
Old (n=20)	Female (n=10)	66.75 \pm 15.28 (53-88)	70.2 \pm 5.35(63-77)
	Male (n=10)	70.5 \pm 7.68 (64-85)	66.8 \pm 11.84(54-85)

Table 5.2 Ages (mean \pm SD, range in brackets) and number of subjects (n), of the skill-immediate (n = 10) and skill-delayed (n = 10)

Age group	Gender	Skill-immediate	Skill-delayed
Young	Female	24.6 \pm 4.7 (21-30) n = 3	23 \pm 1(22-24) n = 3
	Male	25.5 \pm 6.3 (21, 30) n = 2	26 \pm 4.2 (23,29) n = 2
Old	Female	63 \pm 5.6 (59,67) n = 2	70.5 \pm 24.8 (53,88) n = 2
	Male	73 \pm 10.4 (67-85) n = 3	68 \pm 4.6 (64-73) n = 3

Participants were recruited through written advertisement in a local paper or following presentation of the project during organized meetings given at social clubs or learning groups. Interested participants were provided with a detailed information sheet (Appendix 1). They were contacted by the researcher 1 or 2 weeks later to discuss any questions or concerns. They were then asked to confirm if they were interested in participating in the project. If they were, the first appointment was made, during which the project was discussed again and time was given for further questions. The relevant measurement tools were introduced and then the participants filled a questionnaire that detailed the exclusion criteria (Appendix 2). Participants were then asked for informed consent (Appendix 3) and the baseline session was carried out.

Exclusion criteria

Exclusion criteria included a history of neurological disorder (stroke, traumatic brain injury, MS, etc.) and/or muscular disorder, history or presence of swallowing disorder, and/or history of head and/or neck surgery or injury. In addition, participants who took medications that might have an impact on swallowing were excluded (such as antipsychotic and anticholinergic drugs). If there were any medical problems that might have had an impact on participation, participants were asked to report this information. The participants were asked to report any history of gastroesophageal reflux disease (GERD). In case of such a report, the researcher further enquired regarding the severity and past interventions. Participants were included if the symptoms were mild and not frequent and were managed with proton pump inhibitor medications, since no differences have been identified in UES resting pressure and nadir pressures during swallowing between people with and without GERD (Kwiatek, Mirza, Kahrilas, & Pandolfino, 2009; Oelschlager, Chang, Pope, & Pellegrini, 2005).

Although TMS has been proven to be safe in the general population (Chokroverty et al., 1995), people with intractable seizures and people with stroke or other types of brain damage may be increased risk of seizures following TMS (Anand & Hotson, 2002; Classen et al., 1995; Wassermann, 1998). Thus, further exclusion criteria were included in the questionnaire based on the Transcranial Magnetic Stimulation Adult Safety Screen (TASS) (Keel, Smith, & Wassermann, 2001). These included the existence of personal or family history of seizures, frequent or severe headaches, metal implants in or around the head, cardiac pacemakers and pregnancy. Other exclusion criteria, like history of stroke or neurological disorders, were included as well as reported above.

5.1.1 Two-week protocol

Participants in this study took part in a training protocol that included 10 training sessions. This training protocol documented changes in the outcome measures following two weeks of either skill or strength training. Participants were scheduled for 12 appointments that included assessments and training. All 40 participants took part in this study. Participants were given a \$150 voucher as reimbursement for transportation costs to and from the laboratory. This study was approved by the Upper South A Regional Ethics Committee, New Zealand.

Participant discontinuation

Two participants did not complete the study. One participant could not finish the study due to increased anxiety following a swarm of earthquakes in Christchurch (commencing September 2010). Another participant dropped out after the first assessment session after commenting that the assessments were perceived as intrusive. Those two participants were replaced by two other participants.

5.1.2 Four-week protocol

The 4-week protocol constituted a pilot study that documented the effects of an increased dosage of training on the outcome measures. The inclusion of such a group arose from a principle of motor exercise regarding increased intensity (*Chapter 3*) and Dobkin's suggestion regarding the use of a pilot study to establish the optimal dose for rehabilitation intervention (Dobkin, 2005).

Participants already involved in the 2-week study were approached by the researcher and were invited to participate in this extended study. This suggestion was given towards the end of the first week of training or at the beginning of the second week. Participants who showed interest were given an additional information sheet (Appendix 4). They were given several days to decide if they were prepared to proceed with the extended training. If they agreed, they completed another consent form (Appendix 5) and nine additional sessions were scheduled on top of the 12 appointments previously scheduled for the 2-week trial (21 in total). Ten participants took part in this pilot study (SKL-I $n = 4$, SKL-D $n = 3$, STR $n = 3$). The participants were given an extra \$100 voucher as reimbursement for their additional travelling costs. All participants recruited to the pilot study completed all sessions. This study was approved by the Upper South A Regional Ethics Committee, New Zealand.

5.2 Assessment Instrumentation

5.2.1 MEP Instrumentation

Three surface electrodes (neonatal solid gel electrodes, BRS-50K, Blue Sensor™, Ambu, Denmark) were placed on the skin following cleansing the submental muscle area with alcohol swabs (isopropyl alcohol 70% v/v Medi-Swab, BSN Medical, VIC, Australia). The electrodes were connected to a shielded cable (Shielded Bio Amp cable, MLA2540, ADInstruments, Castle Hill, Australia) which was connected to an EMG amplifier (Dual Bio Amp™, ML135, ADInstruments, Castle Hill, Australia) (see Figure 5.1). The EMG amplifier was plugged in to a custom-built triggering device¹ that was connected to the data acquisition system that recorded the data (Powerlab™ 8/30, ML870, ADInstruments, Castle Hill, Australia) (see Figure 5.1). The recording system then transferred the data to the data acquisition software (Scope™ version 3.9.1, ADInstruments, Castle Hill, Australia) supplied with the PowerLab hardware. Scope was used to receive, display, and record the data to the computer. Data was acquired at a 10 kHz rate, using a high-pass filter at 10 Hz and a low-pass filter at 2 kHz.

The triggering device (see Figure 5.1) was used to monitor to stream of the sEMG signals following amplification and send those signals to the PowerLab recording system. In addition, the triggering device was connected to the output trigger of the transcranial magnetic stimulator. This device was manually set to trigger at a threshold that represented 75% of each participant's mean submental sEMG peak amplitude of 10 non-effortful swallows recorded using the same hardware, software, and settings. Once the threshold was reached, the triggering device produced a single transistor-transistor logic (TTL) impulse. This impulse signalled the TMS coil to discharge, via the connection between the triggering device and the transcranial magnetic stimulator. In addition, the triggering device signalled the recording software to save 100 ms of data immediately before the TMS stimulator discharged and collect 160 ms of data immediately after the TMS stimulator discharged. Overall, each sweep (recording period) was 260 ms in duration. Following each TTL impulse, the triggering device was disabled for a 30 s period that allowed the participant to rest and prepare for the next sweep. During this rest period, an indicator light, placed on the front panel of the triggering device that could be seen by both the researcher and the participant, was automatically switched on. Once the 30 s passed, the light switched off, indicating that the

¹ Swallowing Stimulator, R. Dove, Department of Medical Physics and Bioengineering, Canterbury District Health Board, Christchurch, New Zealand, 2007.

triggering device was again receptive for monitoring the EMG signal, and again, once the pre-set threshold was breached, the TMS coil discharged via its connection to the triggering device. If the threshold was not breached, the TMS coil did not discharge the magnetic pulse and activity was not recorded. Similar settings of the recording system, triggering device and magnetic stimulator have been used in other studies from our laboratory (Abdul Wahab et al., 2010; Doeltgen et al., 2010; Doeltgen, Ridding, et al., 2009; Macrae, 2011).

For setting up the threshold for the triggering device, recordings of 10 non-effortful saliva swallowing were acquired while the triggering device was disabled, with the light indicator used to prompt the participant to swallow saliva every 30 s. This allowed the participant to practice swallowing to the visual signal. In addition, the Scope software display of waveforms was used as a biofeedback modality to allow the participant to practise submental muscle contraction needed for the tasks.

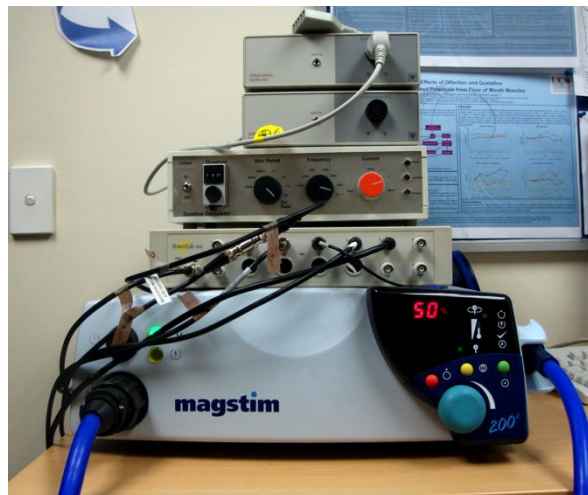


Figure 5.1 From top: two EMG amplifiers with shielded cable connected to the top unit, the triggering device, PowerLab, Magstim unit.

TMS of the primary motor cortex associated with the submental muscles was conducted using a figure-of-8 coil with an outer wing diameter of 70 mm (see Figure 5.2) with a magnetic stimulator unit with a maximal output of 2.2 Tesla (Magstim 200TM, Magstim Company Limited, Whitland, Wales) (see Figure 5.1). The Magstim 200TM unit produces a pulse with a rapid time of 150 μ s from onset to peak with 90% of the discharge occurring during the first 100 μ s, and a decay time of 1 ms from peak to zero (Nollet, 2003).

MEP analysis software

A custom-designed software package² was used to measure the onset and magnitude of MEPs. Data from the Scope software were recorded as Scope files (.sfwdat) and then saved as text files which could be used in the University of Canterbury (UC) Evoked Potential Analysis software (version 3.15). The software displayed each MEP in a separate window, with an option for displaying the rectified ensemble average waveform of multiple MEPs that was used in this study. Onset and offset latency markers could be either subjectively placed or automatically placed based on a specified criterion. The magnitude of the MEP was calculated as the area under the waveform between the onset and offset of the time markers.



Figure 5.2 Figure-of-8 coil.

5.2.2 Pharyngeal Manometry instrumentation

The manometry and EMG equipment was connected to the KayPENTAX Swallowing Signals Lab (KayPENTAX Inc., Lincoln Park, NJ, USA). The manometry catheter was 100 cm in length and 2.1 mm in diameter with solid-state unidirectional sensors (Model CTO/2E-3, Gaeltec Ltd., UK). The catheter housing contained imprinted numbers, which signified its length from tip to 50 cm, in 5 mm increments. Thus, measurement of the catheter depth, once inserted, was available. The catheter is embedded with three 2 mm wide x 5 mm long pressure sensors and one EMG electrode at the following locations: the most distal sensor is 2.7 cm from the tip of the catheter, the second sensor is 2.2 cm proximal to the first sensor, and the third sensor is 1.3 cm proximal

² University of Canterbury Evoked Potentials Analysis Software, G. A. O'Brien, Department of Communication Disorders, University of Canterbury, New Zealand 2010.

from the second, and 4.3 cm proximal from the most distal sensor. The EMG electrode is embedded midway between the 2nd and 3rd sensors, at midway but was not utilized in this study (see Figure 5.3).

The catheter was calibrated at room temperature at 250 mmHg using a calibration kit (Hand held digital RS232 manometer, model 8205, pressure range 0±5 psi, accuracy of ±0.3% of full scale). Pressure data were converted to a digital signal of 12-bit samples and a sampling frequency of 500 Hz. All waveforms were displayed on a computer monitor using a 250 mmHg high and 30 s long display during data collection. The waveforms were digitally recorded for later analysis.

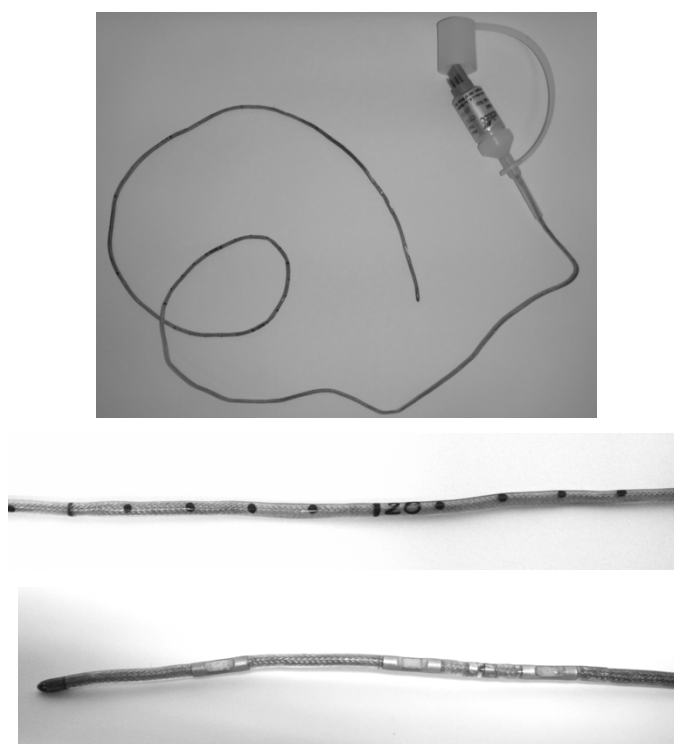


Figure 5.3 Top: manometry catheter, middle: distance marking imprinted on the catheter, bottom: three embedded pressure sensors.

5.2.3 sEMG instrumentation

Submental sEMG signals were obtained using a single disposable circular patch containing three silver/silver chloride electrodes (disposable pre-gelled electrode pad, Multi Bio Sensors Inc., El Paso, TX, USA) arranged in a triangular configuration. Two electrodes were designated for recording and the third was used as ground. The patch was 58 mm in diameter, with inter-electrode distance of 20 mm from the centre of each electrode and 10 mm distance from the internal lateral edges.

The sEMG signals were recorded and processed using the KayPENTAX Swallowing Signals Lab (KayPENTAX Inc., Lincoln Park, NJ, USA). Sampling frequency for sEMG signals was 500 Hz. The raw signal was band-pass filtered (50-250 Hz), integrated (time constant = 50 ms), and rectified.

5.2.4 Ultrasonography Instrumentation

A Siemens ultrasonography device (Model: Acuson Antares Premium Edition, Siemens Medical Solution USA, Inc., Mountain View, CA, USA) was used with 2 types of transducers: 13-5 MHz linear array transducer and 6-2 MHz curved array transducer.

The linear array 13-5 MHz transducer (Figure 5.4) was used to obtain cross-sectional area images of the submental muscle group when placed in the coronal plane under the chin. Image settings of depth (cm), frequency (MHz), 2D gain (dB), resolution/speed, map type, tint, SieClear property, edge sharpness, number and location of focus points, and shape of the beam were all individually set for each participant to achieve an optimal image and were recorded.



Figure 5.4 Linear array 13-5 MHz transducer.

The curved array 6-2 MHz transducer (Figure 5.5) was used to obtain images of hyoid displacement from the mid-sagittal sub-mandibular location. This location allowed visualization of the submental muscle group in the middle of the image, and the mandible spine and hyoid bone at the image edges. Each swallowing event was recorded using a 5 s long video clip but longer recording loops were available if needed. Again, the image settings were individually set for each participant to achieve an optimal image. The resolution/speed setting was set to obtain a high rate of frames-per-second, but the number of frames acquired during the video clip was also dependent on other settings like frequency and number of focus points. Thus, the number of frames-per-second changed between participants, as well as the other image settings. The settings used for

each participant were recorded. Aquasonic 100 Ultrasound Transmission Gel (Parker Laboratories Inc.) was applied on the transducer to improve ultrasound transition from and to the transducer by serving as a conductive medium.



Figure 5.5 Curvy array 6-2 MHz transducer.

To avoid neck flexion and to maintain the consistent head and transducer position at baseline and outcome sessions (Chi-Fishman, 2005), a custom-made stabilization stand was used (Figure 5.6) (Macrae, 2011). The stand was composed of a 1 m² platform to which an upright metal pole was fixed close to the lateral edge. A chair was positioned on the base, facing the pole (Figure 5.6), and was fixed by two wooden holders placed at the front two legs of the chair (Figure 5.7). The pole had two horizontal metal arms, top and bottom, that were adjustable in height along the pole and in depth towards the chair (Figure 5.6). The arms could be fixed in place by screwing in a bolt. The arms had measurements imprinted on them (at 0.5 cm intervals), so that once fixed in place, a measurement of depth could be taken. A measurement tape was secured along the length of the pole (Figure 5.7), so once the arms were fixed, a measurement could be taken regarding each of the arms' height.

The top arm was used to stabilize the head and neck by attaching a customised dental bite block for each participant. The bite block was attached to the distal aspect of the arm such that the participant could bite onto the bite block. The bottom arm was used to stabilize the transducer (Figure 5.8). The handle of each transducer was encapsulated in a custom-made metal case. The case was tightly fit around the transducer by an internal lining of putty that eliminated gaps between the transducer body and the metal case (Figure 5.9). The metal case could be bolted to the bottom arm of the stand. Its attachments allowed for vertical movements of the case in relation to the arm (left to right in relation to the person sitting on the chair) and also allowed for an

angular movement of the case, from a perpendicular position of the transducer in relation to the ground, to approximately 60 degree towards the chair (Figure 5.10).

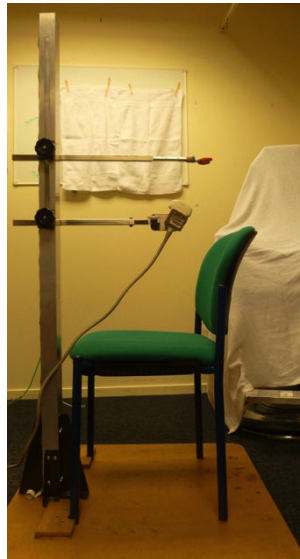


Figure 5.6 Stabilizing unit: base platform, chair, metal pole, horizontal arms.



Figure 5.7 Wooden holders placed at the front of the chair and measurement tape on pole.

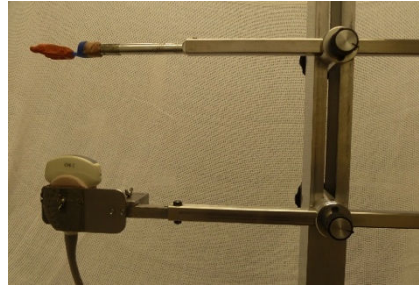


Figure 5.8 Stabilizing unit: top arm: bite block with dental impression; bottom arm: transducer (in metal case).

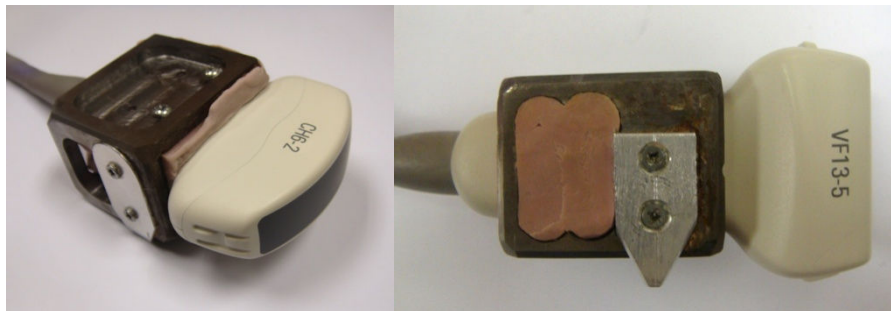


Figure 5.9 Transducers in metal case: left 6-2 MHz, right: 13-5 MHz transducers.

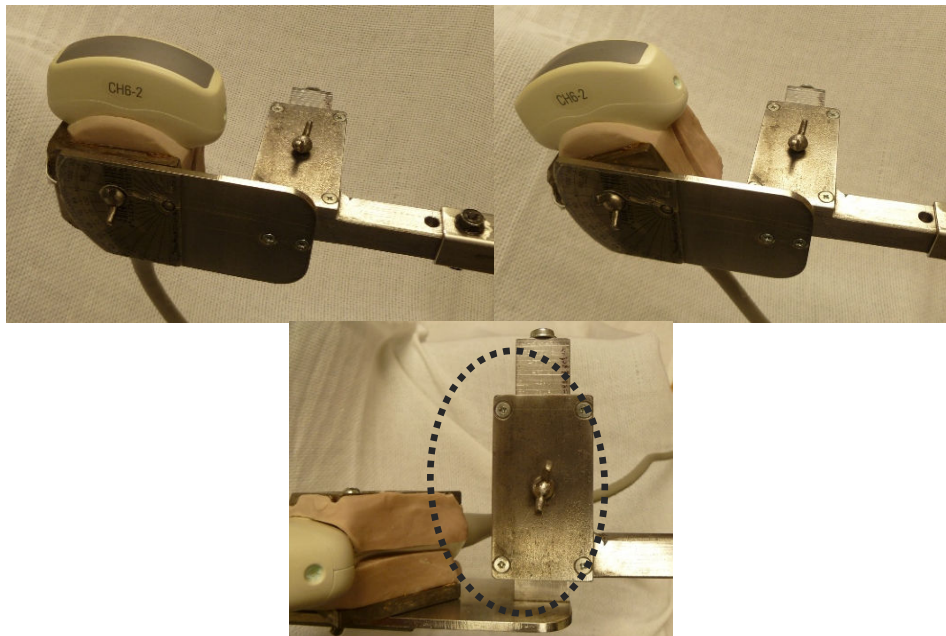


Figure 5.10 Bottom arm, top picture: left and right: demonstrating angular movement of the transducer, bottom pictures: vertical movement adjustments.

5.2.5 Swallowing training questionnaire

Logemann (2005) mentioned the importance of documenting the compliance to swallowing training among healthy older adults by collecting comments regarding exercise performance, in addition to noting the rate and reason for lack of compliance. Thus, a questionnaire (see Appendix 6) was used in this study as well. The questionnaire was written by the researcher and intended to document complaints, pain during training, enjoyment levels (and thus motivation), and subjective functional changes in swallowing.

5.3 Biofeedback in Swallowing Skill Training Software Programme (BiSSkiT)

BiSSkiT was developed by the research team³ to meet the goals of this research project. Software development took approximately 8 month.

5.3.1 BiSSkiT - Software design

The software was written in PythonTM, an open-source programming language that can run on Windows, Linux/Unix, and Mac. It accepted data streams from a portable EMG device (MyoPace, Model NE-1, Niche Technology Ltd, New Zealand; Input range: 0.2-1000 μ V, bandwidth 100-200 Hz) and plotted the data as waveforms in real time on the computer screen (ViewSonic Model VS12825, 17 inch).

BiSSkiT offered a skill-training option that included a target area of a quadrangular shape; and a strength-training option that included a horizontal bar that served as the target. Both training options utilized sEMG biofeedback from the submental muscle area.

The software was designed to offer several configuration options that could be accessed through the software code or through the graphical user interface (GUI). In addition, it offered the option to set default configurations to achieve uniformity among participants in each group of training.

The GUI configuration options include customizing the following options:

1. Training type: skill or strength

³ Concept: Maggie-Lee Huckabee, Code writing: Ben Han, Software development: Oshrat Sella, Ben Han, Richard Jones and Maggie-Lee Huckabee.

2. Session options: number of trials per session, number of trials per block, duration of breaks between trial-blocks (in seconds) and each trial duration (in seconds).
3. Plot options: Y axis maximum value during calibration, background colour, plot line colour & width, strength bar colour & width, skill target colour.
4. Strength training options: target increments (percentage), hit tolerance, miss tolerance.
5. Skill training options: target increments (percentage), hit tolerance, miss tolerance, fixed target aspect ratio (square or rectangle), fading schedule options, delayed feedback options.

In addition, the GUI offered options for opening a new file or an existing file, saving data to the computer, and exporting data to a comma-separated values (CSV) file.

Exporting data

Two CSV files were created for every session. The first included information of the rectified and smoothed EMG data at its sampling rate of 10 Hz. The second file included information about the session configuration and values of each trial performance: the amplitude, timing and size of the target (for skill) and the amplitude of the target (for strength), the timing, and the amplitude of the swallow, and hit or miss information. In addition, the following information was averaged for each of the five blocks (20 trials) and for the whole training session (100 trials): hit rate (for skill), mean peak and maximum peak. The CSV files were saved and could be opened in an Excel spreadsheet.

5.3.2 BiSSkiT - Application

The output port of the MyoPace portable sEMG device had a cable with three alligator clips connected to a sEMG electrode (5.2.3) placed on the submental area. Prior to electrode placement, the skin under the chin was cleaned with alcohol swabs. The two recording surface electrodes were placed in an anterior-posterior position on the external mid-sagittal plane of the mandible, underlying the floor-of-mouth muscle group. Hence, the electrical activity was collectively registered from right and left anterior belly of digastrics, right and left mylohyoid, and right and left geniohyoid. The anterior electrode was placed approximately 2 cm from the mandibular spine, and the second recording electrode 1 cm posterior to it. The ground electrode was oriented laterally to the recording electrodes. During positioning of the recording electrodes, the participant was asked to keep a neutral head position to avoid neck extension.

The default settings were chosen to be 100 trials per session, divided into five blocks of 20 trials each, with a 100 s long break.

At the beginning of each session, a calibration process was performed. The participant was asked to perform five effortful swallows, with a 30 s rest between repetitions. The average of those five swallows (the calibration value) was used as a reference for additional settings:

- For strength training: the initial amplitude of the target matched the calibration value. The Y axis values ranged from 0-220% of the calibration value.

- For skill training: the initial size of the target, at its X axis, was 50% of calibration value. The Y axis matched the X axis to form a target shaped as a square. The target was placed along the screen in various locations according to the following configurations: the lower limit of the target was 20% of the calibration value. This meant that the lower edge of the target could not be placed below this threshold. The upper allowable limit was 70% of the calibration value, meaning that the upper edge of the target could not be placed above this threshold. Thus, height-wise, the target could be placed anywhere between 20% – 70% of the calibration value. In addition, a 2 s margin was used so that the target could be placed between 2 s – 28 s along the screen. The Y axis values range was 0-120% of the calibration value

Since the primary goal was not the measure the influence of biofeedback on outcomes – but rather to measure the influence of 2 different types of training (skill and strength) – using biofeedback in only one type of training (skill) might have confounded the result by introducing another variable to training type. Therefore, use of biofeedback across both types of training programmes allowed for control of the potential confound of feedback presence on targeted tasks.

In addition, both training approaches utilized adaptive procedures to determine the characteristics of the next trial, depending on ‘success’ (‘hit’) and ‘failure’ (‘miss’) of prior responses. This concept was adapted from the psychophysical evaluation literature (Leek, 2001). The *staircase procedure* is a simple and flexible procedure that has been widely used for assessing threshold or performance level (Leek, 2001; Levitt, 1971). This procedure is based on using the previous response in order to determine the next trial goal, and at the end, a threshold estimate is given. In the *transformed* version of the staircase procedure, a sequence of the responses (negative or positive) is used to determine the next trial target or threshold, as opposed to the *simple staircase procedure* in which the difficulty level changes in response to every trial. Use of sequences of two, three, four responses or more, have been reported in the past (Levitt, 1971). In this study, three consecutive negative responses (in three consecutive trials) reduced the next trial demand (whatever that may be, depending on the training type); and three consecutive positive responses

increased the next trial demand. Using the same adaptive procedure in both training types was done to avoid another confounding variable. Since determination of ‘success’ and ‘failure’ followed the same rules in both training, motivation was better controlled. In addition, the ‘step size’ (Leek, 2001) had to be determined. The step size is the amount of change between one target to the subsequent target. This amount was randomly chosen after trialling the software, with a change of 10% of the current target selected. The rationale was that the increase should not be too small or too large. The 10% increment/decrement was used for both training types to avoid confounding and uncontrolled variables.

5.3.2.1 *Strength training*

The target for strength training was chosen to represent maximal contraction, based on the assumption that strength training should introduce a demand for high level of force production and that demand should be increased over time in order to encourage the occurrence of adaptive changes, as discussed in *Chapter 3: Literature Review – motor learning*. Strength training utilized the effortful swallowing technique. Since effortful swallowing, as its name suggests, required swallowing with effort. To introduce increasing demand the initial target was calibrated at the beginning of every training session and the target threshold was increased based on possible increases in force production of the targeted muscles.

The software provided targets in the shape of horizontal bars that crossed the screen. As the participant demonstrated increase strength during swallowing, the height of the bar increased, thus increasing the demand for strength. A ‘hit’ was defined as a trial in which the peak of the waveform touched the bar (had the same amplitude) or was above the bar (had higher amplitude than the bar). A ‘miss’ was defined as a trial in which the peak of the waveform was below the bar (was lower in amplitude than the bar’s amplitude). A ‘miss’ was therefore a result of insufficient strength relative to the demand introduced by the bar.

After three successive ‘hits’ the height of the bar increased by 10%, or after three ‘misses’ the height of the bar decreased by 10%. If the participant performed a pattern of hit-miss-hit-miss or miss-miss-hit-miss for example, the size did not change, until three consecutive hits or misses occurred. This was done in order to achieve mastery at a certain level of difficulty before continuing to the next level of difficulty.

Figure 5.11 presents an example for an initial target in strength training, and Figure 5.12 presents an increase of the target height in the amplitude axis (Y axis) (i.e., increasing demand for strength by raising the bar).

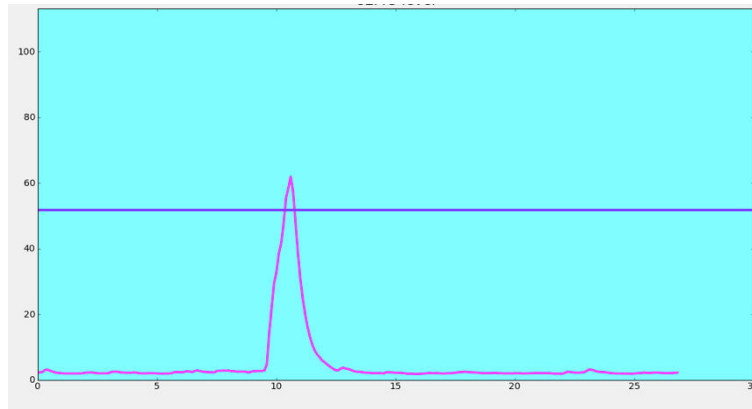


Figure 5.11 Screen shot - strength training.

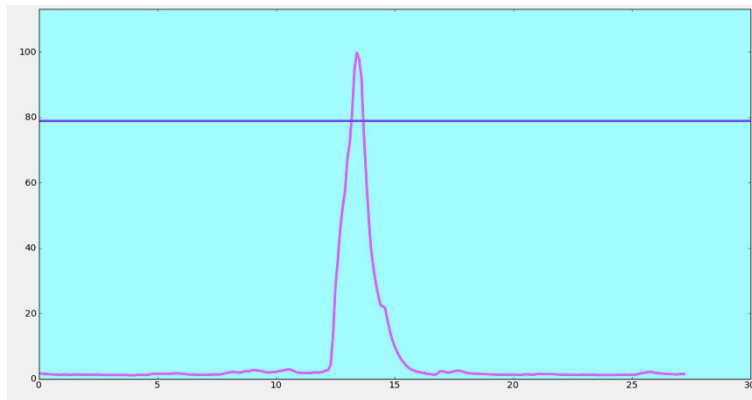


Figure 5.12 Screen shot - strength training.

5.3.2.2 Skill training

Skill training consisted of a target that varied in two dimensions: strength and timing that had to be met in order to reach precision. As precision of movement was improved, the target decreased in size, thus increasing the demand for further improvements in precision. Hence, a larger target area will allow more ‘room’ for imprecision, and a small target will allow less ‘room’ for imprecision. The target was randomly placed on the screen. For example, in one trial, the target could have been placed in the lower left corner, demanding low strength but fast reaction time, and in another trial, the target could have been placed at the top right corner of the screen, demanding more force but with a longer preparation time. A *hit* was defined as trial in which the peak of the waveform fell somewhere within the target area. A *miss* was defined as a trial in which the peak of the waveform fell outside the target area. A *miss* can be a result of mistiming, with swallowing occurring too early or too late in relation to the target box location. A *miss* can also be a result of imprecise amplitude, with the swallow being too strong or too weak relative to

the target box; or, it can be a result of imprecision in either or both dimensions, which exceeded the amount of leeway allowed (i.e., the size of the target).

During skill training, the amplitude requirements were set to be between 20-70% of the calibration value. The upper limit was chosen based on the assumption that changing the demand for force within a wide range, is sufficiently challenging to cause adaptation; previous research has suggested that simply repeating an action is not enough to cause change in the neural substrate (Plautz et al., 2000). However, increasing the upper limit to more than 70% of maximal strength would have introduced a demand more closely resembling strength training, which was not the intention of this type of training. Lowering the threshold below 20% was found to be difficult during software trials for due to a technical reason of signal noise. Since the amplitude of the waveform at rest (no swallowing) was not set exactly at zero, a target that was lower than 20% might have been 'hit' by facial or lingual movement not associated with pharyngeal swallowing. For example, participants had to use their tongue to collect saliva between trials, and this could have raised the EMG level to that of the target had it been lower than 20% of the calibration value.

In addition, the skill training paradigm provided the option of immediate or delayed visual feedback. The immediate feedback protocol allowed the participant to see the waveform throughout the entire trial. The delayed feedback protocol training enabled the participant to see the waveform only after a certain amount of time following performance. A time delay of 2 s was chosen based on existing literature that suggests that the time gap should not be too long to allow forgetfulness to occur, nor too short to allow for inhibit adequate time for cognitive processing of the internal sensation accompanying the motor act (see *Chapter 3: Literature Review – motor learning*). In the delayed feedback option, the participant could only see a vertical time cursor as it dynamically moved along the screen, from left to right (from time 0 s to 30 s) and symbolized the point of the leading edge of the waveform. If the task was performed with adequate temporal precision, swallowing should have occurred by the time cursor passed the target. Visual feedback of the waveform amplitude was given 2 s after the waveform passed the right edge of the target, beyond which the waveform stayed visual until the end of the trial. Since the 2 s as measured from the right border of the target area, the delay between the peak and the feedback varied. Figure 5.13, Figure 5.14 & Figure 5.15 demonstrate the application of the skill with the delayed visual feedback protocol.

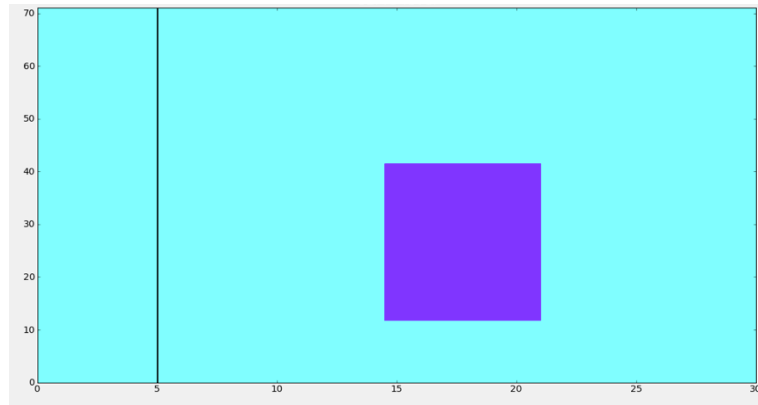


Figure 5.13 Screen shot - skill training with delayed visual feedback.

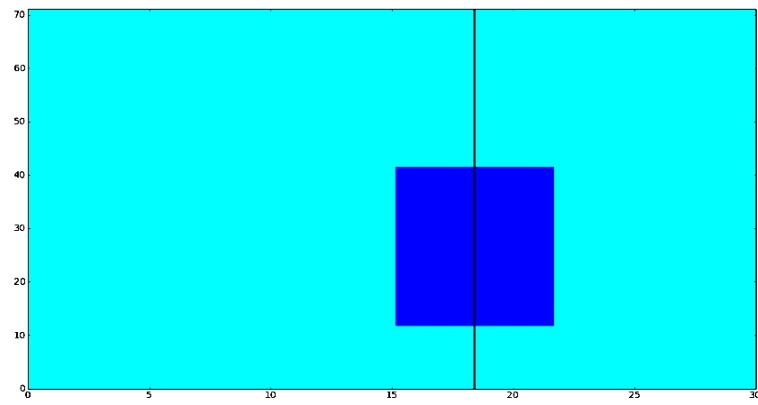


Figure 5.14 Screen shot - skill training with delayed visual feedback.

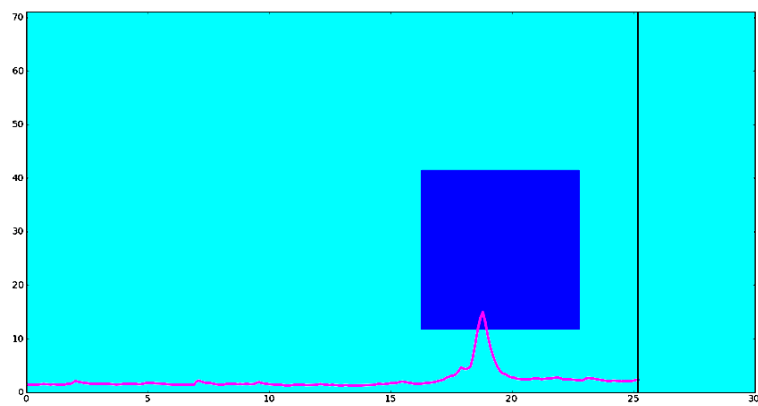


Figure 5.15 Screen shot - skill training with delayed visual feedback.

Figure 5.16 and Figure 5.17 demonstrate a decrease in target area with increased precision.

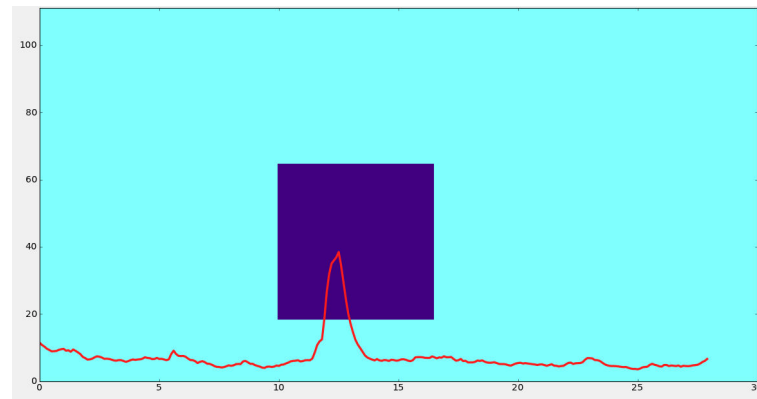


Figure 5.16 Screen shot - skill training with immediate visual feedback.

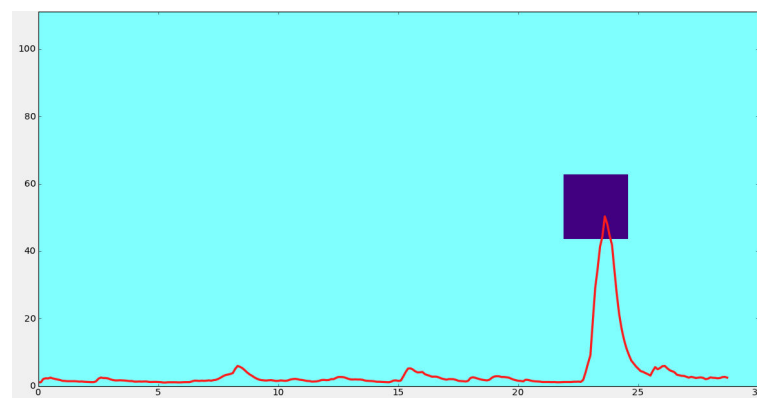


Figure 5.17 Screen shot - skill training with immediate visual feedback.

5.4 Overall organization of the two training protocols

Participants attended the Swallowing Rehabilitation Research Laboratory located at the New Zealand Brain Research Institute (formally known as the Van der Veer Institute), where all the assessment and training sessions took place. Each participant was seen individually. Before attending the first baseline session, participants were assigned to one of the two training groups. Assignment was done in a counter-balanced manner, to match the two groups for age and gender. Each subject received a random 5-digit number serving as an I.D. Data sheets were coded using each subject I.D., and during data entry and analysis, the researcher was blinded to groups and subjects. In addition, following subject allocation into groups, the subjects were informed regarding the task requisites, but not the group name ('Skill' or 'Strength').

5.4.1 Two-week protocol

Each participant was seen for 12 sessions (Table 5.3). The initial session included baseline measurements and was carried out during a time period of 3-12 days prior to the first training session. Table 5.5 presents the assessment and training protocol. The baseline session included several assessments:

1. Excitability of the cortical projections to the submental muscle group was assessed using single-pulse TMS over the submental-related hotspot of the motor cortex during two tasks: volitional saliva swallowing and volitional submental muscle contraction. The evoked motor response was registered from sEMG electrodes located over the submental muscle group and was later analysed for magnitude (Chapter 6 and Chapter 9) and latency (Chapter 9).
2. Pharyngeal pressure was assessed using a manometric catheter that had three pressure sensors embed, to allow assessment of the oropharynx, hypopharynx, and UES during four types of tasks: non-effortful saliva swallowing, non-effortful 10 mL water swallowing, effortful saliva swallowing, and effortful 10 mL water swallowing. Amplitude and duration measurements were later analysed.
3. Submental muscle activity was assessed concurrently with pharyngeal manometry, and muscle activity was registered using the same four tasks. Surface EMG electrodes were located over the submental muscle group. The EMG waveforms were later analysed for amplitude.
4. Hyoid displacement was assessed during saliva swallowing using B-mode real-time ultrasound images recorded as video clips. A curvy transducer was placed at the mid-sagittal plane, under the mandible.
5. The CSA of the anterior belly of digastric and geniohyoid muscles were measured during rest using B-mode real-time ultrasound image taken with a linear transducer placed at the coronal plane under the mandible.

Training was provided 1 hour a day, 5 days a week, for 2 weeks. The skill training group focused on swallowing precision and the strength training group focused on enhancing the strength of swallowing. Both groups used sEMG biofeedback utilizing BiSSkiT (Section 5.2.5) to facilitate mastery of training goals. The training was given individually and all training sessions were monitored by the researcher.

The first training session was carried out on a Monday and lasted for an hour. Immediately following the training MEPs were measured during volitional swallowing and contraction at 5, 30, 60, and 90 min after training. This was done in order to assess the immediate effects of 1 training session on neurophysiological excitability over a 2-hour time period. On the next day (Tuesday) the second training session took place. The following training sessions (3-9) took place in successive days, excluding the weekend (Saturday & Sunday). The 10th training session was carried on a Friday. Again, similarly to the first training session, immediately following the 10th training session, the participant was taken to the examination room where MEPs were measured during volitional swallowing and contraction at 5, 30, 60, and 90 min after training. This was done in order to assess the cumulative effects of 10 training sessions on neurophysiological excitability over a 2-hour time period.

Four days after the 10th training session (i.e., Tuesday), the outcome session was carried out. The same assessments undertaken at the first baseline session were repeated in order to document the cumulative outcomes of the training on the neurophysiological, biomechanical and muscular levels.

At the end of the outcome session, the participants were given their reimbursement payment. After that, the swallowing training questionnaire (Appendix 6) was given to the participants before leaving the research facility. Participants were given 10 min to complete the questionnaire and were asked to leave it on the table.

Table 5.3 Timetable of appointments at the laboratory, including the procedures and length of each meeting (2-week protocol)

Baseline session	First training session + MEPs session	Training sessions: 2 nd -9 th	10th training session + MEPs assessment	Outcome session (2 weeks)
Any day of the week, 3-12 days before the 1 st training session	Monday	Week 1: Tuesday-Friday Week 2: Monday-Thursday	Friday	Tuesday
MEPs Ultrasound Manometry sEMG	Training MEPs (2 hr)	Training	Training MEPs (2 hr)	MEPs Ultrasound Manometry sEMG
3 hr	3 hr (1 hr + 2 hr)	8 hr (8 sessions*1 hr each)	3 hr (1 hr + 2 hr)	3 hr

5.4.2 Four-week protocol

The procedure used in this study was very similar to the one described for the 2-week protocol, with the following exceptions. Participants interested in participating carried on with the same training they were doing (either skill or strength). Thus, assignment into groups was not controlled, and the groups were consequently not balanced for age or gender (see 5.1.2).

Each participant was seen for 21 sessions overall, thus 9 sessions were added (Table 5.4). The description of the first 12 sessions is given above. Following the outcome session (Tuesday), the 11th training session was scheduled the day after (Wednesday). Again, the training sessions (11th - 18th) were scheduled on consecutive days, excluding the weekend. The 18th training session was followed by immediate MEP assessment session, similarly to the first training session. Again, MEPs were measured during volitional swallowing and contraction at 5, 30, 60, and 90 min after training. This was done in order to assess the cumulative effects of 18 training sessions on neurophysiological excitability over a 2-hour time period.

The final outcome session was scheduled 4 days after the 18th training session, hence on a Tuesday. The same assessments completed during the first baseline session and the two-week

outcome session were repeated, in order to document the cumulative outcomes of the extended training on the neurophysiological, biomechanical, and muscular levels.

As before, at the end of the outcome session, the participants were given their reimbursement payment. After that, the swallowing training questionnaire (Appendix 6) was given to the participants before leaving the research facility. Table 5.6 presents the 4-week training and assessment protocol.

Table 5.4 Timetable of appointments at the laboratory, including the procedures and length of each meeting (4-week protocol)

Training sessions: 11 th -17 th	18 th training session + MEPs assessment	4 weeks outcome session
Week 3: Wednesday-Friday	Friday	Tuesday
Week 4: Monday-Thursday		
Training	Training MEPs	MEPs Ultrasound Manometry sEMG
7 hr (7 sessions*1 hr each)	3 hr (1 hr + 2 hrs)	2.5 hr

Table 5.5 Two-week training and assessment protocol

		3-12 days										4 days			
	Baseline	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6	Session 7	Session 8	Session 9	Session 10	Outcome (post 2 weeks training)			
MEP	15 swallowing 15 contraction	5 min post									5 min post		15 swallowing 15 contraction		
		30 min post									30 min post				
		60 min post									60 min post				
		90 min post									90 min post				
Pharyngeal Manometry	5 non-effortful saliva											5 non-effortful saliva			
	5 non-effortful 10 mL											5 non-effortful 10 mL			
	5 effortful saliva											5 effortful saliva			
	5 effortful 10 mL											5 effortful 10 mL			
Submental sEMG	5 non-effortful saliva											5 non-effortful saliva			
	5 non-effortful 10 mL											5 non-effortful 10 mL			
	5 effortful saliva											5 effortful saliva			
	5 effortful 10 mL											5 effortful 10 mL			
Hyoid movement	5 non-effortful saliva											5 non-effortful saliva			
Submental CSA	1 still image											1 still image			
Performance: hit rate		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
Performance: sEMG peak		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
Questionnaire												✓			

Table 5.6 Four-week training and assessment protocol

		1 day							4 days		
	Outcome (post 2 weeks training)	Session 11	Session 12	Session 13	Session 14	Session 15	Session 16	Session 17	Session 18	Outcome (post 4 weeks training)	
Submental MEP	15 swallowing								5 min post		15 swallowing
	15 contraction										15 contraction
									30 min post		
									60 min post		
Pharyngeal manometry	5 non-effortful saliva								90 min post		5 non-effortful saliva
	5 non-effortful 10 mL										5 non-effortful 10 mL
	5 effortful saliva										5 effortful saliva
	5 effortful 10 mL										5 effortful 10 mL
Submental sEMG	5 non-effortful saliva										5 non-effortful saliva
	5 non-effortful 10 mL										5 non-effortful 10 mL
	5 effortful saliva										5 effortful saliva
	5 effortful 10 mL										5 effortful 10 mL
Hyoid movement	5 non-effortful saliva										5 non-effortful saliva
Submental CSA	1 still image										1 still image
Performance: hit rate		✓	✓	✓	✓	✓	✓	✓	✓		
Performance: sEMG peak		✓	✓	✓	✓	✓	✓	✓	✓		
Questionnaire											✓

5.5 Assessment procedures

5.5.1 MEP procedures

Participants were seated on a comfortable chair in the examination room. The skin under the chin and over the zygomatic arch was cleaned using alcohol swabs. Two surface electrodes were placed on the external midsagittal plane of the mandible, overlying the floor-of-mouth muscle group (Al-Toubi et al., 2011; Doeltgen et al., 2010, 2011; Macrae, 2011). The electrical activity was therefore registered collectively from the submental muscle group. The anterior electrode was placed first, lining its anterior edge behind the bony edge of the mandible and the lateral edges evenly extended on either side of the midline. The second electrode was placed posteriorly to the first one, with an inter-electrode distance of approximately 10 mm. During positioning of these recording electrodes, the participant was asked to keep a neutral head position and avoid neck extension. By doing this, the researcher ensured proper location, adhesion to the skin and no contact between the anterior and posterior electrodes. In addition, a third sEMG electrode (same as above) was placed over the bony prominence of the cheek (over the zygomatic arch). Following placement, the electrodes were connected to the bio-amplifier.

Determining the triggering device threshold

In order to determine the threshold at which the triggering device generated a TTL impulse that resulted in TMS discharge, 10 volitional non-effortful saliva swallows were collected. The indicator light on the external panel of the triggering device was used to indicate 30 s between each trial. The instruction was “Every time the light turns off, swallow your saliva. Try to swallow with no effort, as you usually swallow”. The data were recorded and the peak amplitudes were calculated immediately after task completion. Then, 75% of the averaged value was calculated and this value was set as the triggering threshold of the device to generate the TTL impulse. This threshold was individually determined for each participant and was used for all MEPs measurements taken from the same participant across all assessments sessions involving MEPs.

Confirming correct task performance

Since data collection included the performance of an unfamiliar task of submental muscle contraction, the participants were allowed to practice this task for approximately 5 min using the sEMG waveform as a biofeedback modality. The instruction for volitional contractions was “Contract the muscles under your chin as if you were trying to stifle a yawn”. Verbal feedback

was given regarding performance. Once the participants manifested control over the task, the next stage of hotspot identification was commenced.

Hotspot identification

First, the vertex (Cz) was marked on the scalp as the intersection of the nasion-inion and inter-aural lines (Klem, Lüders, Jasper, & Elger, 1999). Then, the hotspot (the area in M1 from which the maximal MEP amplitude could be recorded consistently) was identified during submental muscle contraction. During hotspot identification, the connection between the triggering device and TMS was disabled so that the researcher could manually trigger the magnetic stimulation. The stimulation output was set to 50% of maximal output of what and was increased to 60% if no response was registered at 50%. The researcher discharged the TMS over the scalp across an area that extended 4 cm anteriorly and 8-10 cm lateral to Cz, since this area overlays the primary motor cortex (M1). The researcher started on the left hemisphere and instructed to participant to contract the submental muscles. Then the magnetic stimulation was immediately discharged. This procedure was carried out at different locations around the designated M1 area described above in both hemispheres until the scalp-site from which the largest and most consistent MEP was identified. Identification was done by examining the MEPs waveforms presented on the computer screen. In order to determine whether a certain MEP was bigger than another, the size of the MEP (peak-to-peak amplitude) was measured with the Scope software cursors. The identified site was determined as the hotspot for magnetic stimulation to elicit MEPs from the submental muscle group.

Once the hotspot was identified, it was marked on the scalp with a water-soluble marker, to ensure consistent placement of the coil during both tasks. Then, measurements of the location of the hotspot in relation to Cz were taken with a measuring tape and recorded. The angle of the coil's handle was recorded as well by taking a photo of the coil's position over the head. In addition, photos of the mark in relation to the hairline, eye, and ear were taken. Documentation of the hotspot was used for re-location of the same site in subsequent sessions. All MEPs were collected from the same site throughout all assessment sessions.

Stimulus response curve

Once identified, increasing magnetic stimulation levels were used over the hotspot in order to identify the maximal MEP magnitude during volitional submental muscle contraction. During this procedure, the triggering device was enabled and the participant's threshold (75% of the average EMG of 10 swallows) was used to trigger the TMS to discharge. Stimulation started from 30% of the maximal output and was increased by 5% increments to a level in which no increase was seen

in MEP amplitude. Three stimulations were administered at each stimulation level. After reaching a plateau in the MEP response, the maximal MEP amplitude was identified from the recorded traces by measuring the peak-to-peak amplitude using Scope cursors.

Determining the stimulation intensity level

After the researcher identified the maximal MEP amplitude among the traces collected, an MEP response with an amplitude approximately half of the maximal MEP was identified among the collected traces, and the level of stimulation needed to elicit this half-sized MEP noted and confirmed by further stimulation (Abdul Wahab et al., 2010; Al-Toubi et al., 2011; Doeltgen et al., 2010; Doeltgen, Ridding, et al., 2009). The rationale for identifying this half-sized MEP level of stimulation was that this level would optimally provide the opportunity for measuring changes in MEP magnitude, whether it is an increase or decrease, following training. This level of stimulation was recorded and used throughout all MEPs assessment sessions for the specific participant.

Submental activation tasks

MEPs were recorded during two counterbalanced tasks: volitional submental contraction and volitional non-effortful saliva swallowing (Al-Toubi et al., 2011; Doeltgen et al., 2010, 2011; Macrae, 2011). The instructions for these tasks were, respectively, “Contract the muscles under your chin as if you were trying to stifle a yawn” and “Swallow your saliva; try to swallow with no effort, as you usually swallow”. Participants were asked to perform the required task each time the light on the triggering device panel turned off. Similar tasks were used in previous studies

MEP data were collected at baseline and at post-training (4 days after the last training session). Task order was randomized and 15 trials (Doeltgen et al., 2010, 2011; Doeltgen, Ridding, et al., 2009) were collected for each task. Each trial was followed by a 30 s rest. If needed, longer periods of time were used between trials to allow more time for saliva collection for the volitional swallowing task, and for rest between contractions if participants reported fatigue. In addition, MEP data for the two tasks were also collected immediately after the 1st and last (10th) training session in the 2-week training protocol, and immediately after the 18th training session in the 4-week training protocol. Hence, immediately following the training session, submental MEPs were recorded during 15 volitional saliva swallowing and 15 volitional submental muscle contraction at 5, 30, 60, and 90 min after training. In total, this assessment took place over 2 hours during which the participant performed 60 swallows and 60 contractions. Previous research has found that repetition of 15 volitional swallowing and 15 volitional submental muscle contractions at 5, 30, 60, 90 min after baseline measures followed by an hour of rest, do not cause changes in

excitability (Al-Toubi et al., 2011). Thus, the assumption was that this procedure could document training-related changes in excitability of the cortical projections from M1 to the submental muscle group following 1 hour of training.

5.5.2 Pharyngeal manometry procedures

Catheter placement

The catheter was calibrated to atmospheric pressure and to 250 mmHg pressure just before the assessment session using the calibration kit. After hand sterilization, the researcher put on gloves and took the catheter out of the calibration chamber. The manometry catheter was placed into an unanaesthetized nostril, chosen by the participant, using a lubricant gel (Lube Gel, Unitrade International (NZ) Ltd, Auckland) to facilitate passage. The unidirectional sensors were facing the posterior pharyngeal wall during catheter placement and data recording. Placement was facilitated using a pull-through technique (Butler et al., 2009; Hiss & Huckabee, 2005; Huckabee et al., 2005; Huckabee & Steele, 2006; Steele & Huckabee, 2007). As the catheter reached the posterior nasal cavity and its tip touched the posterior pharyngeal wall, as identified by resistance to further insertion, the participant looked towards the ceiling by dropping the head back and extending the neck. In this position there was no structural resistance to further insertion at the nasopharyngeal angle and the catheter was inserted in a further 1-2 cm until it reached the nasopharynx. The participant then returned the head to a neutral position, was handed a glass of water, and was asked to drink the water quickly through a straw. In doing so, the catheter was swallowed through the hypopharynx and through the UES. The depth of insertion was monitored and the subject was asked to stop drinking when the distal catheter was approximately 30 cm from the tip of the nose. The catheter was then slowly pulled back. When the catheter was held stable, intermittent swallowing of saliva was performed by the participants to assess the catheter placement, until the M-wave was identified by visual examination of the waveform of the distal sensor. The M-wave indicated placement of the distal sensor at the superior border of the UES. By locating the lower sensor at the level of the UES, the locations of the top two sensors could be assumed to be approximately at mid-pharynx (the middle sensor) and at the level of the tip of the epiglottis (the uppermost sensor) (Figure 5.18). Once correct placement of the catheter was identified, the catheter was taped to the outside of the nose with medical tape (3M MicroporeTM hypoallergic surgical tape 1533-0) to avoid displacement during swallowing. Catheter reorientation was carried out as necessary during the assessment. Participants were given a few minutes to adjust to the sensation of the catheter before commencing swallowing tasks. This was done since the UES is sensitive to distension (Olsson, Nilsson, et al., 1995), and a short rest is recommended to allow the sphincter to relax and accommodate to the presence of the catheter (Butler et al., 2009). The

naris side (right or left) and the imprinted number (in cm) on the catheter that was measured at the tip of the nose, were noted for each participant and were used for subsequent data collection.



Figure 5.18 Lateral pharyngeal radiographic image with the manometry catheter in situ. Three manometric pressures are shown: (A) position at the tip of the epiglottis, (B) at mid-pharynx, and (C) at the UES [taken from Huckabee & Steele (2006)].

Swallowing tasks

After the participants adjusted to catheter placement, they performed five repetitions of four swallowing tasks:

- Non-effortful saliva swallowing: “Swallow your saliva with no effort; try to perform a regular swallow”.
- Effortful saliva swallowing: “Swallow your saliva with lots of effort, think about swallowing a whole boiled egg at one go, contract all the muscles in your mouth and throat”.
- 10 mL non-effortful water swallowing: “Place the water in your mouth and hold, wait for my cue and swallow the water as you would usually swallow, with no particular effort, just a normal swallow”.
- 10 mL effortful water swallowing: “Place the water in your mouth and hold, wait for my cue and swallow the water with lots of effort, think about swallowing a whole boiled egg, contract all the muscles in your mouth and throat”.

Tap water at room temperature was used for the water bolus. Time between each repetition was 30 s. The four types of tasks were randomized. In total, each participant performed 20 swallows, while the researcher was monitoring the waveforms on the screen for any indication of dislocation of the manometry catheter. If this was detected, the participant was asked to repeat the required task.

5.5.3 sEMG procedures

Prior to electrode placement, the skin under the chin was cleaned with alcohol swabs. See 5.3.2 for description of sEMG electrode placement underlying the floor-of-mouth muscle group. This location was similar to that used for MEPs recordings. Following positioning, the researcher made sure that the EMG signal acquired during rest was not ‘noisy’ (i.e., below 10 μ V in amplitude).

Swallowing tasks

Surface EMG data were collected concurrently with pharyngeal manometry. The same four tasks and instructions were performed, with five repetitions of each and 30 s rest between trials. In total, each participant performed 20 swallows. Tap water at room temperature was used for the water bolus. The four types of tasks were randomized.

5.5.4 Ultrasonography procedures

To avoid neck flexion and maintain consistent position of the head in relation to the transducer, the custom-made stabilizing stand was used. As described before in Section 5.2.4, the top arm of the stabilizing stand held the bite block and the lower arm held the transducer in its case. Prior to data collection, bite blocks were created. The bite block was made of acrylic material (Plaque photo, light-curing hybrid composite resin, W&P Dental, Germany), and shaped in a horseshoe that fit a standard bite (Figure 5.19). Several sizes were pre-cast so the appropriate size could be chosen to fit the participant's bite.



Figure 5.19 Bite block.

Taking the participant's dental impression

The researcher chose one of the pre-cast bite blocks, after examining the participant's bite. In order to create the dental impression, two-component Vinyl Polysiloxane Impression Material Putty (3M ESPE ExpressTM STD) was used. The impression materials were mixed by hand for 30 s until a cohesive mixture was formed. This mixture was spread on both sides of the bite block and with minimal delay (to minimize hardening of the putty), the participant was asked to open their mouth. After the researcher placed the bite block at the midline of the oral cavity and assured proper position of the bite block, the participant was asked to bite down gently on the putty until feeling the hard surface of the bite block. The participant was asked to close the lips around the bite block as possible. The participant held the bite block between the teeth for approximately 4 min, until the putty had set. Then, the researcher used gloves (powder-free micro-textured latex gloves, Healthcare Distributors Ltd, Christchurch, New Zealand) to remove the bite block with the dental impression from the participant mouth. After washing the bite block of saliva, a disposable scalpel (Miltex stainless steel disposable scalpels #10) was used to trim the residual putty in order to improve comfort during oral placement of the bite block. The bite block with the dental impression (Figure 5.20) was placed on the top arm of the stabilisation stand and taped with a medical tape (3M MicroporeTM hypoallergic surgical tape) to assure stability and lack of movement.



Figure 5.20 Bite block with dental impression, after trimming the lateral edges to maximize comfort.

Positioning the participant in the stabilizing stand

The participant was asked to sit on the chair that was placed on the stand base. While sitting, the researcher positioned the chair so that the front two legs of the chair slipped in to the wooden holders. The participant was then asked to sit upright, and make sure their back was aligned and touching the back of the chair. This was done in order to achieve similar positioning throughout the assessments. Once correct positioning was achieved, the top arm was adjusted in height and depth until the bite block was positioned inside the participant's oral cavity. The participant was given time to adapt and further adjustments were made to assure the participants comfort. In a previous study in which the influence of bite block presence on swallowing was measured compared to regular swallowing, the presence of the bite block between the teeth did not affect the timing or duration of tongue and hyoid movement (Gay et al., 1994).

The transducer case was attached to the lower arm. Generous amounts of ultrasound transmission gel were placed on the transducer to improve contact with the skin. The height and depth of the lower arm was adjusted so that the transducer would be in contact with the desired area. Care was taken to ensure that there was no pressure against the skin to avoid muscle deformation (Scholten, Pillen, Verrips, & Zwarts, 2003). Further adjustments were made to assure the participant's comfort. All height and depth measurements, for both the top and bottom arms, were recorded and used in repeated measures from the same participant.

Two types of measurements were taken using ultrasonography: hyoid displacement and the CSA of the submental muscle group. These were counterbalanced in order. The participant had approximately a 5 min period of rest, or more if needed, between the two measurements.

5.5.4.1 *Hyoid displacement*

The curved array 6-2 MHz transducer was used to obtain images from the mid-sagittal plane of the mandible. The angular position and the lateral position of the transducer were adjusted and the images on the screen were monitored until the geniohyoid was seen at the middle of the image and the acoustic shadow of the hyoid bone was seen on one side of the image and the mandible spine at the other side of the image. The pressure of the transducer on the skin was minimized by observing the skin surface and the shape of the muscles on the screen (Scholten et al., 2003). The image settings were then adjusted to obtain a clear image. Once the transducer was set and the image's settings were made, five repetitions of saliva swallowing were performed. The participant was asked to swallow as normal as possible without applying excessive force or pressure during swallowing. Each swallow was followed by a 30 s rest, but if needed, the participant was given more time between repetitions to generate sufficient saliva. Each swallow was recorded using a 5 s video clip. If a longer acquisition time was required due to difficulty in initiating a prompt swallowing response by command, the video clip length was extended to 10 s. The image setting and the transducer position (angular and vertical) were recorded, and used for subsequent measurements.

5.5.4.2 *Submental cross sectional area measurement*

The linear array 13-5 MHz transducer was used to obtain images of submental muscle group cross-sectional area when placed in the coronal plane. The transducer was adjusted so that it was perpendicular to the mandible and approximately midline between the mandibular spine and the superior edge of the thyroid cartilage, without applying excessive pressure over the muscles that might cause deformation (Scholten et al., 2003). While performing the adjustment, the images were monitored on the screen. If the midline position of the transducer caused the digastric muscles (right and left) to get cut out of the image at their external lateral edges, the transducer was moved towards the mandible until both right and left digastric were visible and with gaps between the image's lateral edges and the muscle's lateral edges, so that enough room was present to document any changes of size increase. Then, the image settings were adjusted to achieve a clear image. Once the transducer was set and the image settings were made, the participant was asked to relax the tongue, face, and neck muscles as much as possible while still images of the muscles were taken during rest. Again, the image settings, the transducer position (angular and vertical) and the stabilization unit measures were recorded, and used for subsequent measurements.

5.6 Training procedure

5.6.1 Swallowing training

Half of the participants were allocated for skill training and half for strength training. Both groups used the custom-designed software (BiSSkiT) that utilized sEMG biofeedback from the submental muscle group.

Participants sat on a comfortable chair in front of the computer screen, in a quiet room. The sEMG electrodes were placed as described in Section 5.3.2. The training parameters for each group were set as the default mode in order to maintain uniformity among the participants in each group. Training consisted of 10 practise sessions, each 1 hour long, conducted on consecutive days, 5 days a week for two weeks. Each session was comprised of 100 trials in total. Each trial lasted 30 s and within this time period one saliva swallow was performed. Each 10 min long block (20 trials) was followed by a 1:40 min break (and up to 5 min, depending on the participant's request). On the first day of training, before commencing the session, participants were given verbal instructions regarding their training aim. During the first training session the researcher gave verbal feedback regarding the participant's performance. For example, for a skill trainee: “You have managed to hit the box even though it is very small”, “You almost hit the box but the peak was a bit too high”. For a strength trainee: “That was a very hard swallow”, “You are making great efforts to swallow hard”. On following training sessions, the amount of verbal feedback was decreased gradually and mainly focused on positive feedback when appropriate. Care was taken when providing feedback since the literature suggests that verbal feedback can influence motor performance, and lead to increased force production (Fischer, Belbeck, & Dickerson, 2010) and also influence motivation (Rose & Robert, 2006). Thus, subjects received similar amount of feedback and encouragement from the researcher. All training sessions were monitor by the researcher. The participants had a drink next to them (water, tea, or coffee) and were instructed to drink during breaks or, if needed, shortly after they performed their targeted swallow.

5.6.1.1 Skill training group

Skill training provided practice in precision of movement based on both temporal and amplitude domains. The aim was to develop conscious control of the timing and strength of swallowing. The software provided targets (‘boxes’) for skilled movement. At odd intervals of approximately once every 30 s, a target area appeared in random locations on the screen: the height of the target (amplitude aspect) and its location along the screen (temporal aspect) changed from trial to trial.

The participant was instructed to swallow such that the peak of the waveform (sEMG amplitude) fell within that area. Hitting the target area resulted in decreased target size only after three successive hits (see 5.3.2), thus requiring sustained precision.

Participants in the skill training group were divided into 2 groups: skill training with immediate feedback (n = 10) and skill training with delayed feedback (n = 10) (see Section 5.1.1 for ages and gender). Participants in the skill-immediate feedback group received on-going feedback throughout all training sessions. Participants in the skill-delayed feedback group received immediate feedback in the first two training session in order to create familiarity with the task, and from the 3rd training session onwards, they received delayed visual feedback. The decision to employ immediate feedback in the first two training sessions was indirectly supported by a study that demonstrated that the ability to plan a movement improves following actual performance of the movement (Cunnington, Iansek, Bradshaw, & Phillips, 1996).

5.6.1.2 *Strength training group*

Strength training was based on the implementation of the effortful swallow technique. The aim of this training was to gradually increase the strength of the submental muscle contraction. Submental sEMG provided visual feedback to the participant on the relative strength of muscle contraction associated with swallowing. Although incorporating a potential component of ‘skill training’ via the use of the swallowing act, the training target was unambiguously maximal strength. The participant was instructed to swallow at anytime they wished during the 30 s trial, such that the peak of the waveform (EMG amplitude) would reach or pass the threshold bar.

5.7 Data extraction

5.7.1 *MEP data*

MEP data were analyzed using the UC Evoked Potentials Analysis software. 15 sweeps collected at each time point (baseline, 5, 30, 60, 90 min post 1st training, and 5, 30, 60, 90 min post 10th training, and post-training) for the volitional saliva swallowing and submental contraction tasks. Latency and magnitude were quantified based on the rectified ensemble-average waveform from the 15 sweeps. The extracted data were recorded in an Excel spreadsheet.

The MEP onset latency was determined as the time point (in ms) at which the waveform departed the baseline followed by a rapid constant raise toward a peak. Since MEPs can have multiple peaks (Wassermann et al., 2008), the rapid constant raise of the baseline was sometimes toward the first substantial peak. In order to avoid EMG activity which was non-MEP related, the onset

had to be equal to or greater than 2 standard deviations (SD) above the background (pre-stimulus) EMG level. The pre-TMS stimulation EMG was integrated over the time period 55 ms to 5 ms (50 ms duration) prior to the magnetic stimulation (Doeltgen et al., 2011). This was used to determine the averaged background EMG level and the 2 SD were automatically calculated by the software based on this information. If the time point chosen was less than 2 SD above the background EMG level, the time cursor was moved to the time-point at which this criterion was met.

MEP magnitude was determined as the area (in $\mu\text{V}\cdot\text{ms}$) between the onset latency (see above) cursor and the offset cursor, automatically placed 15 ms after the onset cursor, as suggested in a study that measured MEPs from anterior digastric muscle (Sowman et al., 2009) (Figure 5.21). In addition, since MEPs were collected during volitional activation (either of swallowing or contraction), there was a need to control for the EMG response included in the MEP, which did not represent the MEP-related EMG response. In order to do that, the pre-stimulus baseline EMG area was calculated over 15 ms long time period from -22 ms to -7 ms prior to the magnetic stimulation (Figure 5.22). The length of this pre-stimulus time period (15 ms) matched the duration in which the magnitude of the MEP response was calculated (15 ms). The pre-stimulus area was then subtracted from the MEP to allow quantification of the MEP related response alone (Doeltgen et al., 2011; Macrae, 2011; Pearce, Miles, Thompson, & Nordstrom, 2003). All data were recorded in an Excel spreadsheet.

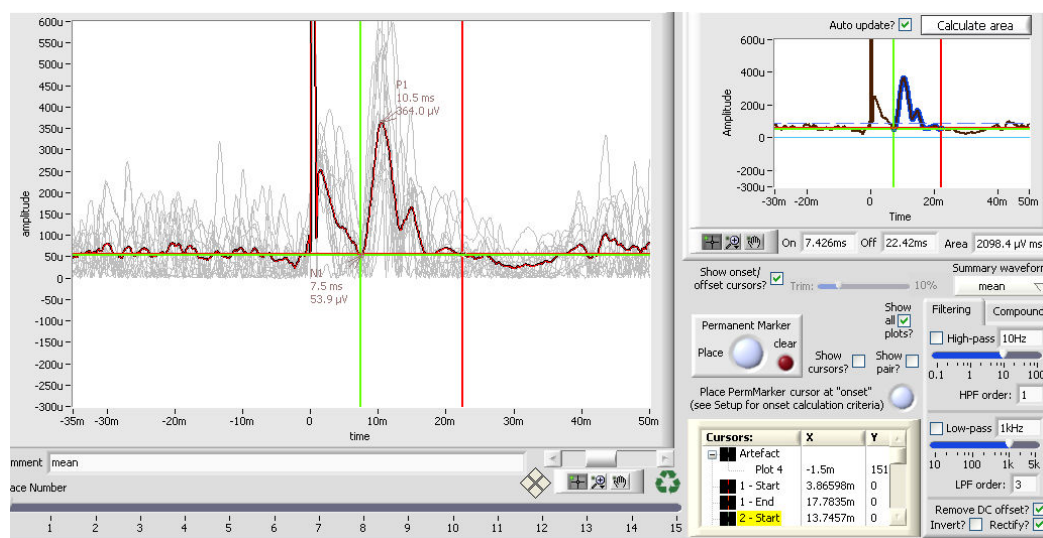


Figure 5.21 Rectified ensemble- averaged waveform. The MEP area post TMS discharge (appears as a thick red line at time 0 ms) measurement between the onset and offset cursors: the green cursor is placed at the onset, and the red cursor 15 ms after the onset.

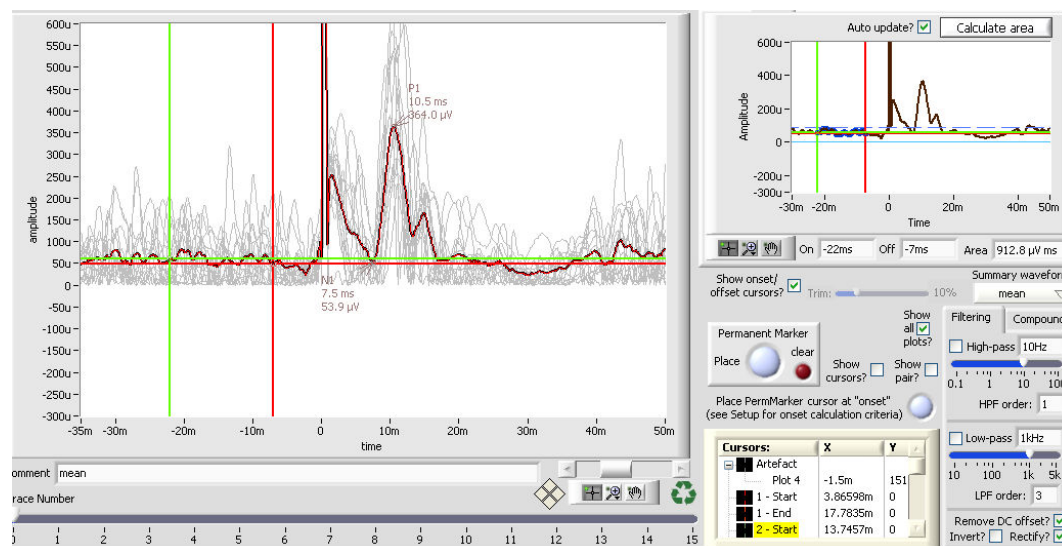


Figure 5.22 Rectified ensemble-averaged waveform. The measurement of MEP area pre-TMS discharge (appears a thick red line at time 0 ms) between the onset and offset cursors: the green cursor is placed at -22 ms, the red cursor at -7 ms.

5.7.2 Pharyngeal manometry data

Manometric waveforms (Figure 5.23) were analysed offline on the KayPENTAX Swallowing Signals Lab. Analysis was done in a 5 s display that stretched the waveform and in a 100 mmHg – 250 mmHg amplitude display to allow increased resolution of the waveform during analysis.

Pharyngeal peak contract pressure was defined as the highest point of the waveform, and UES nadir pressure as the lowest point of the waveform, measured in mmHg. These measurements were calculated automatically by the workstation computer, by manually selecting the waveform of interest and then using the ‘waveform statistic’ option. The maximum and minimum peak values of the selected waveform were displayed.

Duration measurements were calculated for each of the three sensors separately (absolute duration measurements). In addition, relative durations between pharyngeal and UES pressure events were calculated to assess for synchronization. The relative duration measurements were calculated in relation to the pressure event of sensor one. All duration measurements were derived in ms and were obtained by using the keyboard pad to highlight the time frame of interest, while monitoring the time and amplitude values. All values were recorded in an Excel spreadsheet.

Absolute duration measurements

The onset and offset time points were determined manually. For the two pharyngeal sensors, the onset time point was determined as the time point at which the waveform departed the baseline followed by a rapid constant raise toward the peak. If there was a slow increase followed by a decrease, or a small increase followed by a plateau, the onset point was determined to be at the time point that was characterized by a constant and rapid upstroke toward the peak, after these events (Figure 5.24).

The offset time point for the two pharyngeal sensors was determined as the time at which the waveform returned to the baseline, following a rapid decrease in pressure. If the pressure showed a drop but without a consistent decrease and without immediately returning to the baseline pressure, then the offset was determined as the time point of the lowest pressure that followed the consistent drop in pressure, but was preceded by an extended pressure period that was up to 15 mmHg above the baseline.

For UES duration measurements, the onset time point was the highest pressure point that preceded a drop in pressure toward the lowest pressure point that was usually characterized by a negative value. The offset time point was the first highest point in pressure that followed the pressure drop.

Relative duration measurements

Onset to onset: the duration between the onset of the upper pharyngeal sensor (sensor 1) and the onset of middle pharyngeal sensor (sensor 2), and the duration between the onset of sensor one to the onset of sensor 3 were measured as the time (in s) between those time points, with sensor 1 serving as the reference point or contrast. If the onsets at sensor 2 and 3 (UES) preceded the onset in sensor 1, a negative value (in s) was assigned. If the onset at sensors 2 or 3 occurred after the onset of sensor 1, a positive value in seconds was assigned. If the onset time points were the same, a 0-s value was assigned.

Peak to peak: the duration between the peak pressure point of sensor one and the peak pressure point of sensor two and also the duration between peak of sensor one to the peak of sensor three were measured as the time in seconds between those time point, with sensor one serving as the reference point or contrast. If the peak in sensor two or three preceded the peak in sensor one, a negative value in seconds was assigned. If the peak in sensors two or three occurred after the peak of sensor one, a positive value in seconds was assigned. If the peak time points were the same a 0-s value was assigned.

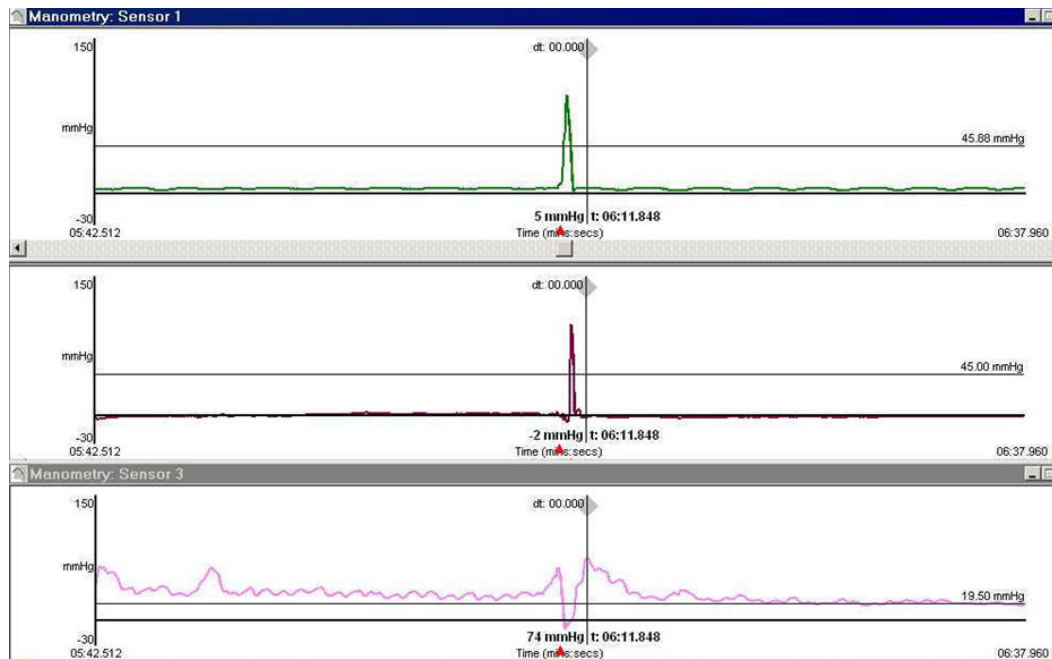


Figure 5.23 Manometry waveforms collected during swallowing (60 s display). Top panel displays the uppermost sensor waveform located at the level of the tip of the epiglottis; middle panel displays the middle sensor located at mid-pharynx; bottom panel displays the lower sensor located at the upper border of the UES. The typical M wave is seen in this waveform.

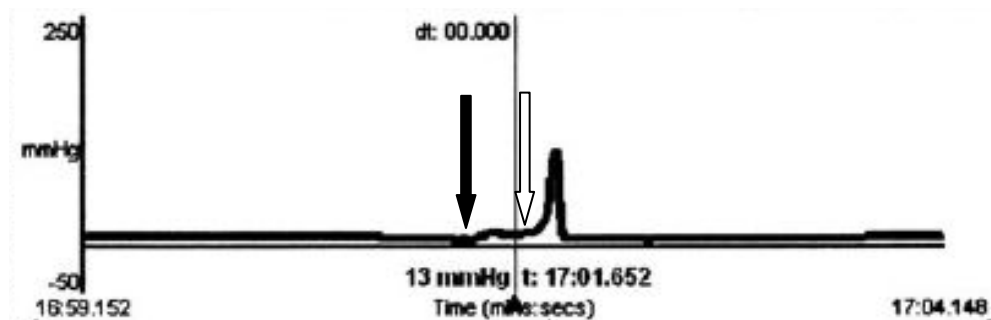


Figure 5.24 Manometry waveform of a pharyngeal sensor (5 s display). An example of an increase followed by a plateau at the onset of the pressure event (black arrow). The grey arrow is pointing to where the onset was determined. [Figure adapted from Huckabee & Steele, 2006].

5.7.3 sEMG data

EMG waveforms were analyzed offline. Analysis was done in a 5 s display that stretched the waveform in an individually-adjusted amplitude display that allowed clear visualization of the waveform during analysis.

The peak of the EMG signal was defined as the highest point of the waveform associated with changes in concurrently measured manometric pressures. This allowed certainty that the change in waveform was indeed swallowing-related. The maximum amplitude was measured in μV and was calculated automatically by the workstation computer, by manually selecting the waveform of interest and then using the ‘waveform statistic’ option. The maximum peak value was then displayed. All values were in an Excel spreadsheet.

5.7.4 Ultrasonography data

All images were imported to a desktop computer (iMac, 27 inch, Apple™) and analysed using OsiriX™, open source software for image processing. The software allows enlarging the image and changing its gain (darken or lighten the image), so as to maximize image clarity.

5.7.4.1 Hyoid displacement

Analysis of the hyoid movement was based on the methods of a recent study (Macrae et al., 2012).

Two points were identified subjectively:

1. The mental spine of the mandible was the *stable reference point*. The intersection of the acoustic shadow and the mental spine of the mandible (black) and the geniohyoid (grey) at its more superficial aspect (closer to the skin rather than the tongue) was the specific location that was marked and served as the reference point.
2. The hyoid bone was the *moving point*. The intersection of the hyoid shadow (black) and the geniohyoid muscle (grey) at their deeper aspect was marked and served as the mobile point.

Two further positions were identified among the video clip images: the rest position of the hyoid, identified as the image that had a maximal distance between the mandible and the hyoid (Figure 5.25), and the maximum displacement of the hyoid identified as the image that had the minimum distance between the hyoid and the mandible (Figure 5.25). The image that contained the rest position and the image that contained the maximum displacement position were analysed.

Electronic callipers were used to measure the distance between the reference point and the mobile point. Thus, two distances were obtained: a rest distance and a maximal displacement distance. This data was entered into Excel spreadsheet. Hyoid displacement was calculated for each of the five video clips, as the percentage of change from rest to maximum (Equation 5.1).

$$\text{Hyoid displacement (\%)} = \left[\frac{\text{Maximal displacement distance (cm)} - \text{Rest distance (cm)}}{\text{Rest distance (cm)}} \right] * 100$$

Equation 5.1 Hyoid displacement calculation

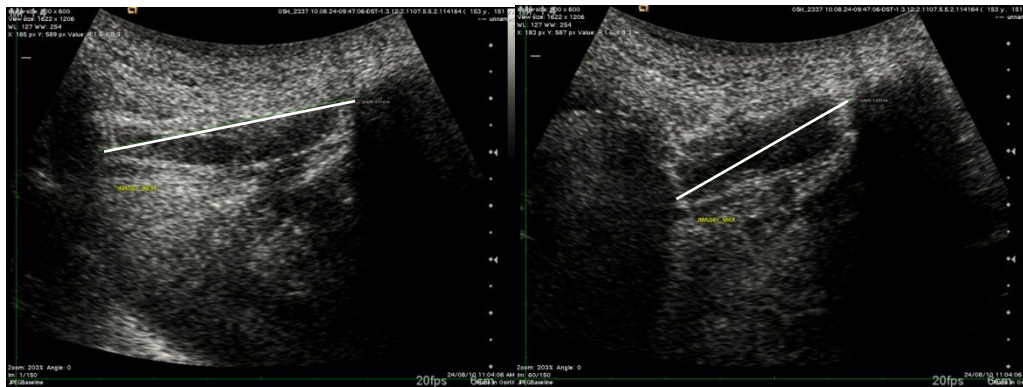


Figure 5.25 Ultrasound images taken at a mid-sagittal plane using the curvy transducer. Right: rest position of the hyoid (hyoid shadow on the left of the white line), left: maximum displacement position of the hyoid.

5.7.4.2 Submental cross sectional area

The muscles of interest were identified and their boundaries were inspected visually. The geniohyoid muscle, which is deeper than the anterior digastric, was difficult to assess and measure since its boundaries were unclear. Thus, it was decided that measurements of the geniohyoid would not be taken.

Continuous trace callipers were used to measure the area (in cm²) of the right and left bellies of anterior digastric (Figure 5.26). Data were recorded in an Excel spreadsheet.

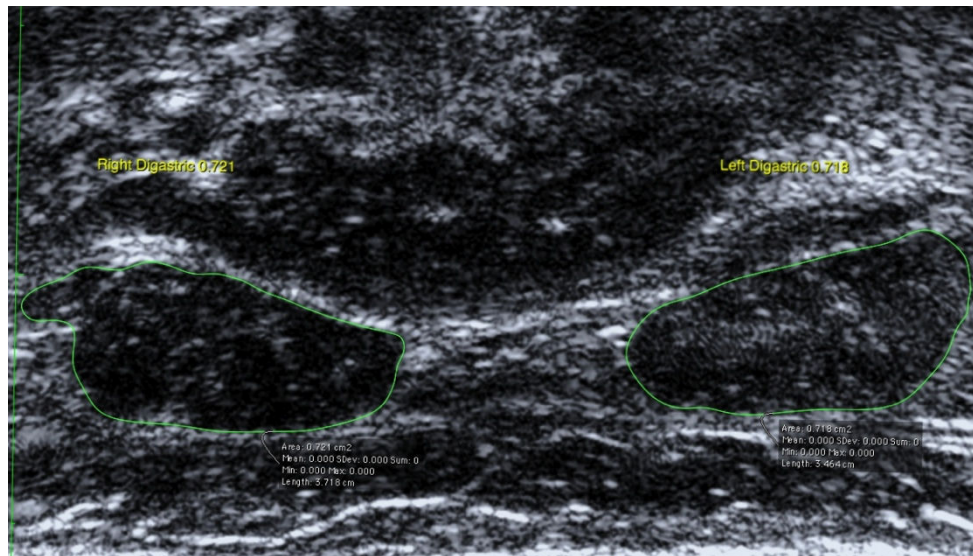


Figure 5.26 Ultrasound images taken in a coronal plane using the linear transducer: Traces around anterior belly of digastric (right and left).

5.7.5 Swallowing training questionnaire

Each of 10 questions was scored on a scale of 1-5 points (1 – strongly disagree, 5 – strongly agree). The 10 questions were divided into four areas:

- A. *Positive questions regarding the experience* (My training was interesting, I enjoyed my training).
- B. *Negative questions regarding the experience* (My training was boring, I disliked my training).
- C. *Positive questions regarding swallowing outcomes* (I feel that my swallowing improved during the training, I feel the training made my swallowing muscles stronger, I feel that the training made my swallowing more accurate).
- D. *Negative questions regarding swallowing outcomes* (I feel that my swallowing deteriorated during the training, I feel the training made my swallowing muscles weaker, I experienced pain during my training).

Each score and comment was extracted into an Excel spreadsheet.

5.7.6 Training performance

The following information was extracted from the CSV file created after every session, for each participant: the session hit rate (the number of trials that contained a target-hit) and the mean of the peak amplitude from sEMG located at the submental muscle area registered for each of the 100 trials. These were collected in an Excel spreadsheet.

5.8 Statistical analyses

Statistical analyses were conducted using SPSS statistics package (IBM SPSS Statistics version 19.0). The overall aim of the main study was to investigate differences between the training groups in the changes of various measures following training. To accomplish that, ANOVA models were used. When data were collected at two time points (e.g., at baseline and following training), the influences of various factors on changes were assessed by calculating the differences in the measure of interest between the two time points (i.e., the value at post 2 weeks *minus* the baseline value). These differences were then entered into the factorial ANOVA model that tested the effects of several factors on the outcome variable. When data was collected at three or more time points (e.g., baseline, 5, 30, 60, and 90 min post training) ‘mixed’ ANOVA was used to examine the differences within- and between-groups. Post hoc analysis was conducted when appropriate.

When comparing SKL to STR, additional factors of gender (Females vs. Males) and age group (Old vs. Young) were entered into the ANOVA model as categorical between-groups factors, and interaction effects between these factors were investigated as well. When comparing SKL subgroups, gender and age group were entered into the ANOVA model as categorical between-groups factors, but due to low number of subjects, only main effects were investigated, without interactions.

The effects of age and gender were included into the model as between-groups factors, due to their effects on the results. Initially, the models used for analyses did not include those two factors. A priori to data collection, hypotheses were formulated under the impression that since the groups were balanced for age and gender, any effect should be eliminated. Thus, the hypotheses for this study focused on training effects rather than the influence of age and gender on training outcomes. However, an additional study (*Chapter 9*) revealed baseline differences in MEPs magnitude between age groups, suggesting that age and gender might play a role in changing training outcomes as well.

Significance value was set at $\alpha \leq 0.05$. All tests were two-sided. Post hoc analyses were conducted when appropriate. Marginally significant results were defined as $0.05 < \alpha \leq 0.10$. Correction for multiple comparisons was not applied due the exploratory nature of this study (Nakagawa, 2004; Phillips, 2004; Robey, 2004a). Confidence intervals (CI) are reported as 95% CI around the mean difference or around the mean, and will appear in the text as CI. Cohen's *d* statistics were calculated to assess effect size. Sphericity was tested for when three or more components (groups, time points) were entered into the ANOVA model. When sphericity was violated, Greenhouse-Geisser correction for degrees of freedom was applied.

For the extended dosage study, descriptive statistic and/or some non-parametric statistical tests was used in order to assess for within-group changes. Comparison between the groups was not possible due to the low number of subjects taking part in this pilot study.

5.9 Inter-rater and intra-rater agreement

The researcher re-analyzed 20% of all data collected from all measurement that were randomly chosen. For inter-rater analysis, an additional researcher analysed randomly-selected 20% of the data collected for all measurements. Inter-rater and intra-rater agreement were analysed using intra-class correlation coefficients (ICC) for each measure.

Table 5.7 ICC for inter-rater and intra-rater agreement

Measure		Inter-rater ICC	Intra-rater ICC
MEP	Area	0.93	0.97
	Onset latency	0.87	0.98
Pharyngeal manometry	Peak amplitude	0.96	1.00
	Durations	0.82	0.96
sEMG	Peak amplitude	0.91	1.00
Hyoid displacement	Percent change	0.81	0.98
Anterior belly of digastric- average	CSA	0.85	0.96
Questionnaire	Training ratings	1.00	1.00
Motor performance during training	Hit rate	1.00	1.00
	sEMG	1.00	1.00

CHAPTER 6: RESULTS

This chapter presents the results of the main study that compared skill to strength training in healthy subjects. In addition, the results of the pilot study that documented the effects of extended dosage of training sessions are presented. Each section consists on the findings of the main study, followed by the findings of the pilot study.

For the main study, each analysis was conducted twice. The first analysis compared differences between SKL and STR training and the model included main effects and interactions. The second analysis compared SKL subgroups (SKL-I vs. SKL-D) but to the small sample size, only main effects were included into the model without interactions. Parametric statistics was used, unless otherwise specified. When the differences in sample sizes were large between the groups (e.g., 10 vs. 20 subjects) non-parametric statistics was used.

Main effects and interactions are presented in tables (referred to in the text) located at the end of each section. Statistically significant and marginally significant effects only are presented in the text.

Effect sizes (Cohen's d) were calculated for each training group (SKL and STR) separately. The changes in a dependent variable are presented for each training group as well, however due to the absence of a control group, it is not possible to quantify order effects unrelated to training, nor to distinguish them from training effects.

Not all of subjects had a full data set for all assessments. Details are provided as to the reason for the missing data and the number of subjects taken into account for each analysis is stated. A summary of all the significant and marginally significant results is presented in Table 6.45, p.277.

6.1 Neurophysiological changes – Submental muscle group MEPs

6.1.1 Two-week training

Data were available from 14 subjects in the STR group and 14 in the SKL group (SKL-I $n = 6$; SKL-D $n = 8$). Of these, 24 had a full data set for all time points for both swallowing and

contraction conditions, one had a full data set for submental contraction only, and three had only submental contraction MEPs with some missing data points due to inconsistent measurable MEPs or MEPs that were outliers in their magnitude. As discussed in Section 2.1.1, in other swallowing studies MEPs could not be elicited in the entire group of subjects recruited (Abdul Wahab et al., 2010; Doeltgen et al., 2010). The exact number of subjects for whom data was used is specified for each analysis.

Due to the small sample sizes of the SKL-I and SKL-D subgroups, an exploratory examination of the data was conducted. The immediate effects of training on MEPs (consisting on one time point that had the largest effect size), and the cumulative effects (i.e., comparing baseline to outcome measures post-training) were examined using non-parametric statistics for SKL subgroups.

6.1.1.1 *Immediate changes post 1st training session*

6.1.1.1.1 *Submental muscle MEPs during volitional contraction*

Four-factor mixed ANOVA with TIME (baseline, 5, 30, 60 and 90 min post 1st session), TRAINING (SKL vs. STR), AGE, and GENDER was conducted (SKL: 8 young and 5 old, 8 female and 5 male; STR: 7 young and 7 old, 8 female and 6 male). There were no significant effects (Table 6.5 p. 186). Cohen's d for effect of training group was 0.49. Figure 6.1 presents the MEP area, by training group, over time. There was a marginally significant main effect of AGE ($p = 0.053$, Cohen's $d = 0.95$) (Figure 6.2), with younger subjects presenting with lower MEP magnitude than older. Effect sizes for each training group (STR and SKL) are reported in Table 6.1.

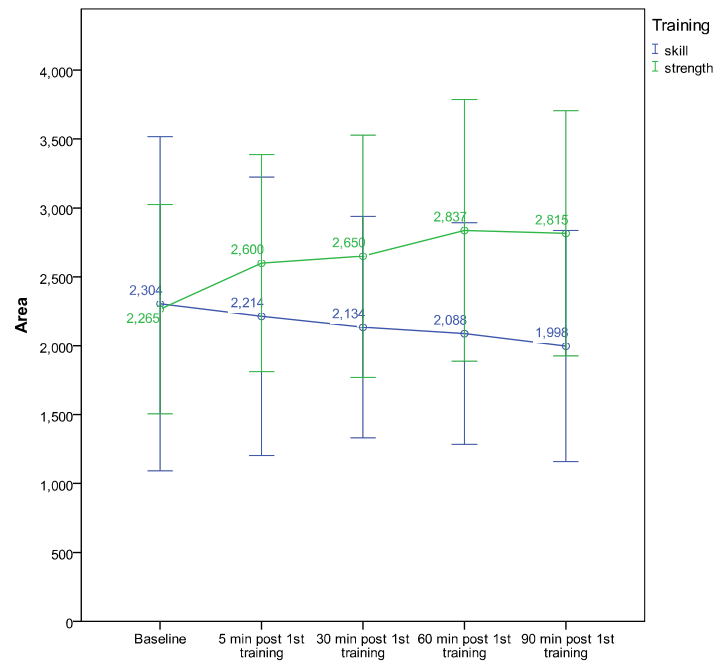


Figure 6.1 Volitional contraction MEP area ($\mu V \cdot ms$): means and confidence intervals, at baseline, 5, 30, 60 and 90 min post 1st training session.

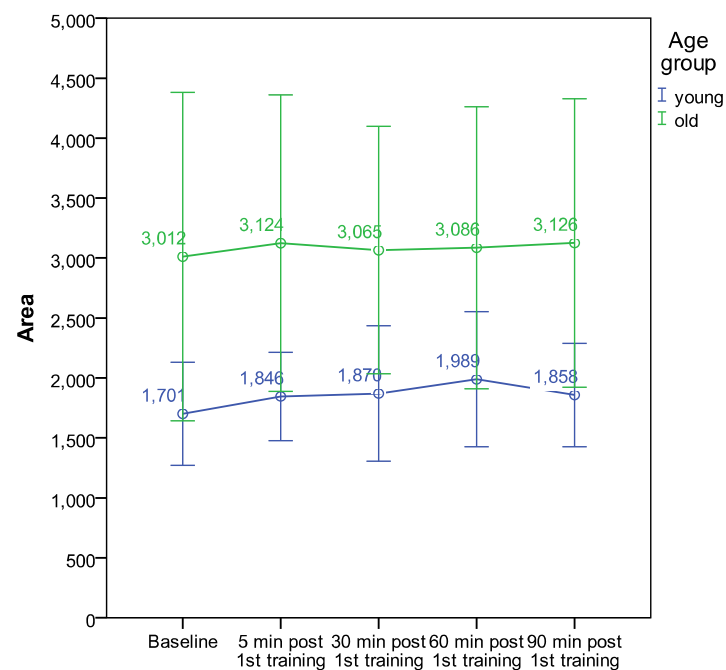


Figure 6.2 Volitional contraction MEP area ($\mu V \cdot ms$): means and confidence intervals at baseline, 5, 30, 60 and 90 min post 1st training session: the interaction of TIME*AGE.

Table 6.1 *Cohen's d for the effect of time on volitional contraction MEPs area: baseline vs. measurement taken at various time points post 1st training session*

	SKL	STR
Baseline vs. 5 min post 1 st training	0.03	0.31
Baseline vs. 30 min post 1 st training	0.12	0.27
Baseline vs. 60 min post 1 st training	0.17	0.37
Baseline vs. 90 min post 1 st training	0.20	0.37

A non-parametric comparison was conducted to find if there was a difference between SKL-I and SKL-D in MEP magnitude measured immediately after the 1st training session (calculated as MEP at 90 min post 1st training *minus* baseline). The time point of 90 min post-training was chosen to be entered to the model following examination of Table 6.1, as it presented with the largest effect size for SKL. Mann-Whitney test for independent samples was used with SKL-I vs. SKL-D as the independent variable and the difference in MEP area as the dependent variable. There was no significant difference between SKL subgroups ($U = 17.00$, $z = 0.439$, $p = 0.66$).

6.1.1.1.2 Submental muscle MEPs during volitional swallowing

Four-factor mixed ANOVA with TIME (baseline, 5, 30, 60 and 90 min post 1st session), TRAINING (SKL vs. STR), GENDER, and AGE was conducted (SKL: 7 young and 5 old, 7 female and 5 male; STR: 6 young and 6 old 7 female and 5 male). There were no significant effects (Table 6.5 p. 186). Effects sizes are reported in Table 6.2 for each training group. Cohen's d for the effect of training group was 0.01. Figure 6.3 presents the results by training group, over time. Cohen's d for the main effect of age group was 0.72. Figure 6.4 present the results by age group over time.

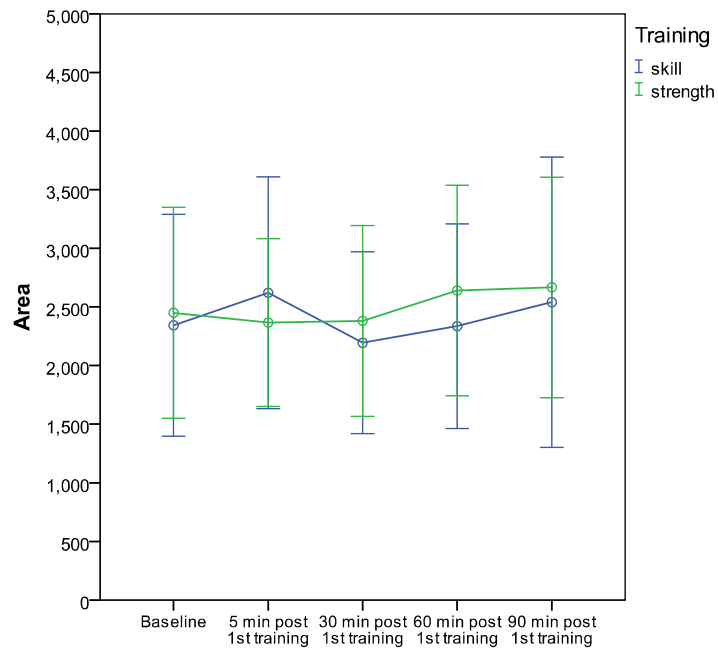


Figure 6.3 Volitional swallowing MEP area ($\mu V \cdot ms$): means and confidence intervals at baseline vs. 5, 30, 60 and 90 min post 1st training session, by training group.

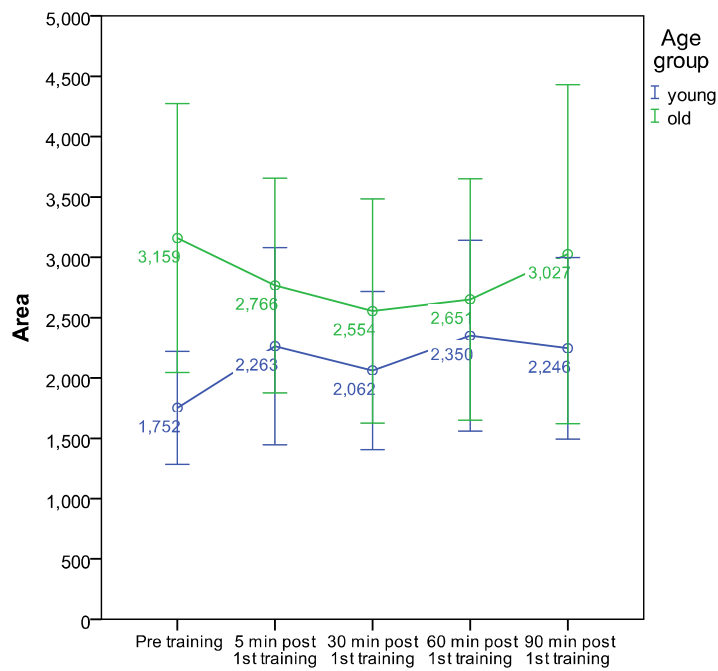


Figure 6.4 Volitional swallowing MEP area ($\mu V \cdot ms$): means and confidence intervals at baseline vs. 5, 30, 60 and 90 min post 1st training session, by age group.

Table 6.2 Cohen's *d* for the effect of time on volitional swallowing MEPs area: baseline vs. measurement taken at various time points post 1st training session

	SKL	STR
Baseline vs. 5 min post 1 st training	0.11	0.07
Baseline vs. 30 min post 1 st training	0.23	0.02
Baseline vs. 60 min post 1 st training	0.14	0.12
Baseline vs. 90 min post 1 st training	0.02	0.17

A non-parametric comparison was conducted to probe for a possible difference between SKL-I and SKL-D in MEP magnitude measured immediately after the 1st training session (calculated as MEP at 5 min post 1st training *minus* baseline). The time point of 5 min post training was chosen to be entered to the model after examination of Table 6.2, since it presented with the largest effect size for SKL. Mann-Whitney test for independent samples was used with the SKL-I vs. SKL-D as the independent variable and the difference in MEP area as the dependent variable. There was no significant difference between SKL subgroups ($U = 19.00$, $z = 0.146$, $p = 0.88$).

6.1.1.1.3 Summary: Immediate changes post 1st training session

To summarize, when assessing immediate changes in MEP area after the 1st training session, there were no statistically significant differences between SKL and STR in MEP area, for either the volitional contraction task or volitional swallowing task.

For the submental contraction task, training group type had a medium effect size. A visual examination of the data indicated that STR had a larger MEP area than SKL, although this difference did not reach significance.

The main effect of AGE produced a large effect size, in volitional contraction ($d = 0.95$). Although the main effect did not reach significance, examination of the data indicated that overall older subjects had a trend towards a larger MEP area than younger subjects.

Effect sizes for the contraction task ranged from very small to small for SKL training. For STR training, the effects were small. For the swallowing task, both SKL and STR had very small to small effect sizes.

6.1.1.2 Immediate changes post 10th training session

6.1.1.2.1 Submental muscle MEPs during volitional contraction

Four-factor mixed ANOVA with TIME (baseline, 5, 30, 60 and 90 min post 10th session), TRAINING (SKL vs. STR), GENDER and AGE was conducted (SKL: 8 young and 6 old, 8 female and 6 male; STR: 7 young and 6 old, 7 female and 6 male) (Table 6.5 p. 186).

There was a significant main effect of AGE ($F(1, 19) = 9.46, p = 0.006$). Figure 6.6 presents the results over time, by age. The mean difference between the age groups was 1239 $\mu\text{V}\cdot\text{ms}$ ($CI [396, 2082]$, Old > Young, Cohen's $d = 1.39$). Old subjects had a mean MEP area of 2880.5 $\mu\text{V}\cdot\text{ms}$ ($CI [2264, 3497]$), while young subjects had a mean area of 1642 $\mu\text{V}\cdot\text{ms}$ ($CI [1066, 2217]$).

There was a marginally significant main effect of TRAINING ($F(1, 19) = 3.11, p = 0.09$, Cohen's $d = 0.79$). The mean difference between the training groups was 710.6 $\mu\text{V}\cdot\text{ms}$ ($CI [-132, 1554]$, STR > SKL). Figure 6.5 presents the results over time, by training group. Effects sizes for the effect of training in each training group are reported in Table 6.3.

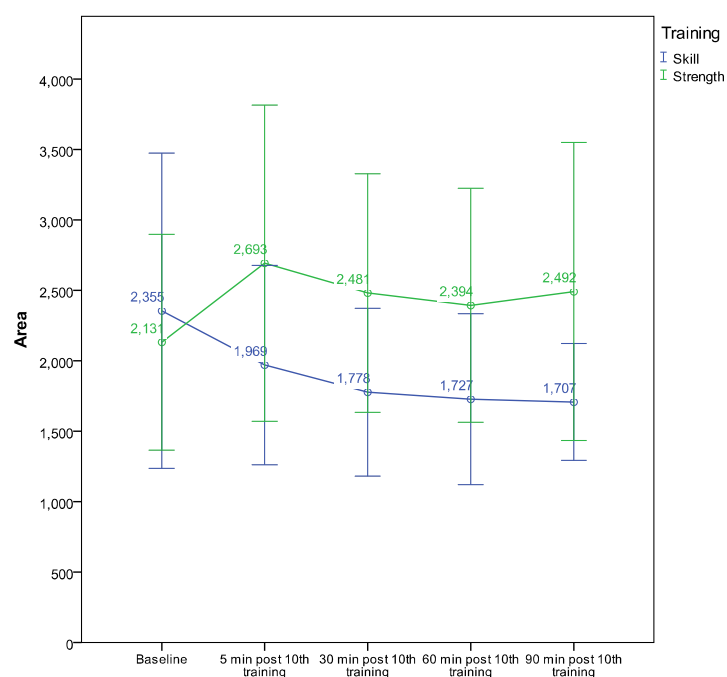


Figure 6.5 Volitional contraction MEP area ($\mu\text{V}\cdot\text{ms}$): mean and confidence intervals at baseline, 5, 30, 60 and 90 min post 10th training session, by training group.

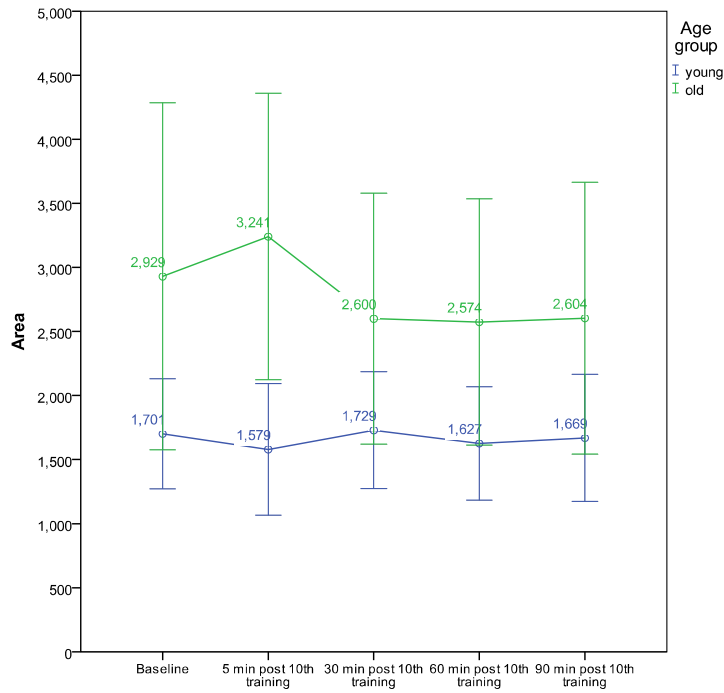


Figure 6.6 Volitional contraction MEP area ($\mu V \cdot ms$): mean and confidence intervals at baseline, 5, 30, 60 and 90 min post 10th training session, by age group.

Table 6.3 Cohen's *d* for the effect of time on volitional contraction MEPs: baseline vs. measurement taken at various time points post 10th training session

	SKL	STR
Baseline vs. 5 min post 10 th training	0.26	0.39
Baseline vs. 30 min post 10 th training	0.41	0.32
Baseline vs. 60 min post 10 th training	0.44	0.30
Baseline vs. 90 min post 10 th training	0.49	0.23

A non-parametric comparison was conducted to explore the difference between SKL-I and SKL-D in MEP magnitude (calculated as MEP at 90 min post 10th training *minus* baseline). The time point of 90 min post training was chosen to be entered to the model following examination of Table 6.3, since it presented with the largest effect size. Mann-Whitney test for independent samples was used with the SKL-I vs. SKL-D as the independent variable and the difference in MEP size as the dependent variable. There was no significant difference between SKL subgroups ($U = 19.00, z = 0.64, p = 0.52$).

6.1.1.2.2 Submental muscle MEPs during volitional swallowing

Four-factor mixed ANOVA with TIME (baseline, 5, 30, 60 and 90 min post 10th session), TRAINING (SKL vs. STR), GENDER and AGE as factors was conducted (SKL: 7 young and 5 old, 7 female and 5 male; STR: 6 young and 6 old, 7 female and 5 male) (Table 6.5 p. 186).

There was a significant main effect of AGE ($F(1,16) = 5.26, p = 0.036$, Cohen's $d = 1.15$) (Figure 6.8). The mean difference was 1121 $\mu V \cdot ms$ ($CI [85, 2157]$). Old subjects had a mean MEP area of 3072 $\mu V \cdot ms$ ($CI [2361, 3782]$) while young subjects had a mean area of 1951 $\mu V \cdot ms$ ($CI [1197, 2704]$).

There was also a significant main effect of GENDER ($F(1, 16) = 5.16, p = 0.037$, Cohen's $d = 1.13$). Figure 6.9 represents the effect of GENDER over time. The main difference between Males and Females was 1110 $\mu V \cdot ms$ ($CI [75, 2147]$). Females had a mean MEP area of 3066 $\mu V \cdot ms$ ($CI [2427, 3706]$) while Males had a mean MEP area of 1956 $\mu V \cdot ms$ ($CI [1141, 2771]$).

There was no significant main effect of TRAINING (Cohen's $d = 0.18$). Figure 6.7 represents the mean MEP area over time for each training group. Effects sizes are reported in Table 6.4 for each training group.

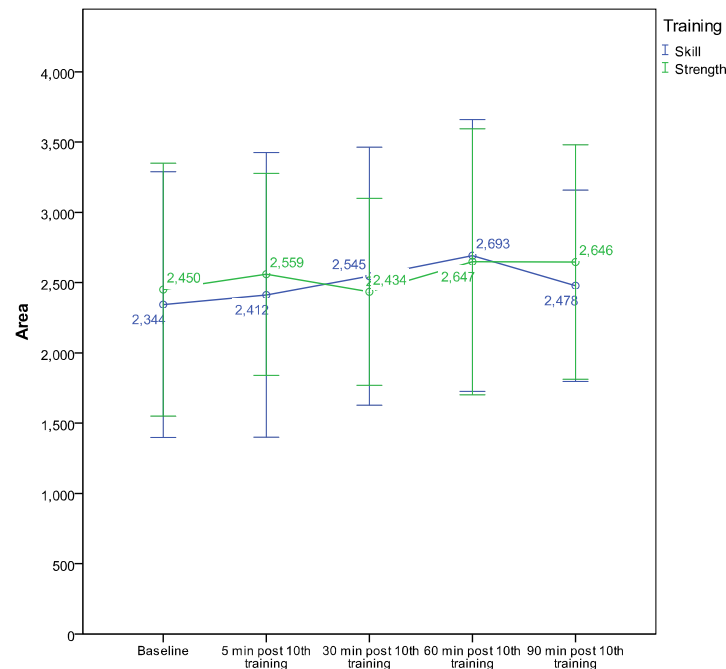


Figure 6.7 Volitional swallowing MEP area ($\mu V \cdot ms$): means and confidence intervals at baseline vs. 5, 30, 60 and 90 min post 10th training session, by training group.

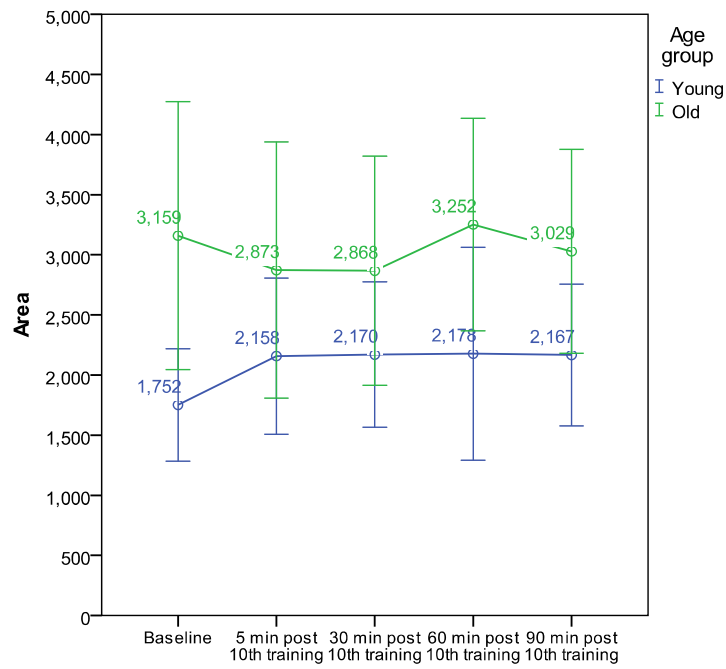


Figure 6.8 Volitional swallowing MEP area (µV*ms): means and confidence intervals at baseline vs. 5, 30, 60 and 90 min post 10th training session, by age group.

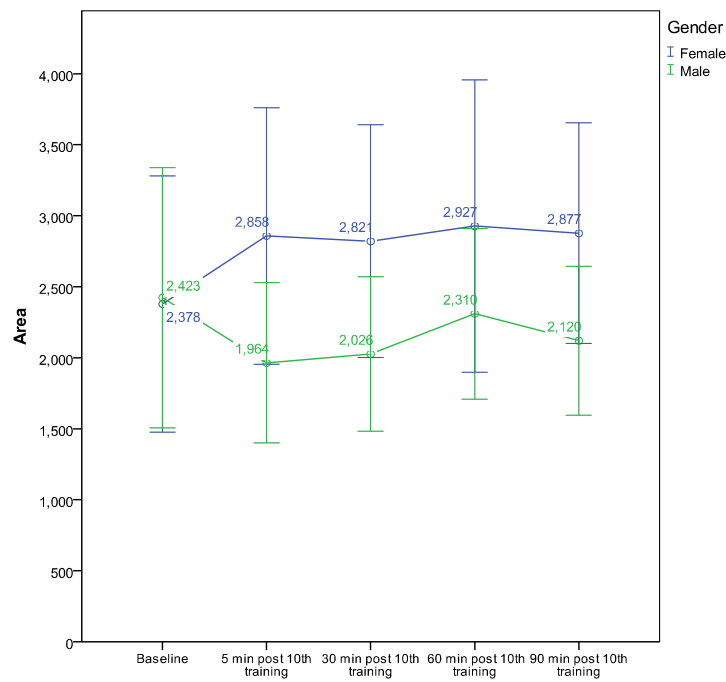


Figure 6.9 Volitional swallowing MEP area (µV*ms): means and confidence intervals at baseline vs. 5, 30, 60 and 90 min post 10th training session, by gender.

Table 6.4 Cohen's d for the effect of time on volitional swallowing MEPs baseline vs. measurement taken at various time points post 10th training session.

	SKL	STR
Baseline vs. 5 min post 10 th training	0.09	0.17
Baseline vs. 30 min post 10 th training	0.00	0.03
Baseline vs. 60 min post 10 th training	0.13	0.27
Baseline vs. 90 min post 10 th training	0.00	0.17

A non-parametric comparison was conducted to explore the difference between SKL-I and SKL-D in MEP magnitude (calculated as MEP at 60 min post 10th training *minus* baseline). The time point of 60 min post-training was chosen to be entered to the model after examining Table 6.4, indicating that 60 min had the largest effect size for SKL training. Mann-Whitney test for independent samples was used with the SKL-I vs. SKL-D as the independent variable and the difference in MEP size as the dependent variable. There was no significant difference between SKL subgroups ($U = 11.00$, $z = 0.85$, $p = 0.39$).

6.1.1.2.3 Summary: Immediate changes post 10th training session

To summarize, when assessing MEP area immediately after the 10th training session (baseline vs. different time points post 10th training session) there were some significant differences. Age had a significant effect in both tasks, with older subjects having larger MEP area than younger subjects ($d = 1.39$ for contraction, $d = 1.15$ for swallowing). Gender had a significant effect in the swallowing task with Females having larger MEPs than Males ($d = 1.13$). For the contraction task, training type produced a marginally significant effect ($p = 0.09$, $d = 0.79$). The data appeared to indicate that there was a trend towards subjects in STR having a larger MEP area than subjects in SKL, although this difference did not reach significance.

The effect sizes for the contraction tasks ranged from small to small-medium for STR training, and from small to medium for SKL training. For the swallowing task, the effect sizes ranged from very small to small for STR. The effect sizes were close to zero from SKL.

6.1.1.3 Immediate changes: 1st session vs. 10th session

6.1.1.3.1 Submental muscle MEPs during volitional contraction

Four-factor mixed ANOVA with TIME (5, 30, 60 and 90 min post 1st session, and 5, 30, 60 and 90 min post 10th session), TRAINING (SKL vs. STR), GENDER and AGE as factors was

conducted (SKL: 8 young and 5 old, 8 female and 5 male; STR: 7 young and 6 old, 7 female and 6 male) (Table 6.5 p. 186). There was a significant effect of AGE ($F(1, 18) = 5.11, p = 0.036, d = 1.07$). The difference between older subjects and younger subjects was $1090.8 \mu V \cdot ms$ ($CI [77.4, 2104.3]$). Older subjects had a mean MEP area of $2854.5 \mu V \cdot ms$ ($CI [2094.7, 3614.4]$), while younger subjects had a mean MEP area of $1763.7 \mu V \cdot ms$ ($CI [1093.1, 2434.3]$).

6.1.1.3.2 Submental muscle MEPs during volitional swallowing

Four-factor mixed ANOVA with TIME (5, 30, 60 and 90 min post 1st session, and 5, 30, 60 and 90 min post 10th session), TRAINING (SKL vs. STR), GENDER and AGE as factors was conducted (SKL: 7 young and 5 old, 7 female and 5 male; STR: 6 young and 6 old, 7 female and 5 male) (Table 6.5 p. 186). There was a marginally significant effect of GENDER ($p = 0.052, d = 1.00$). The difference between Females and Males was $1133 \mu V \cdot ms$ ($CI [-11, 2276]$). Females had a mean MEP area of $3054 \mu V \cdot ms$ ($CI [2348, 3760]$), while Males had a mean MEP area of $1921 \mu V \cdot ms$ ($CI [1021, 2821]$). Figure 6.10 presents the mean MEP area over time, by gender.

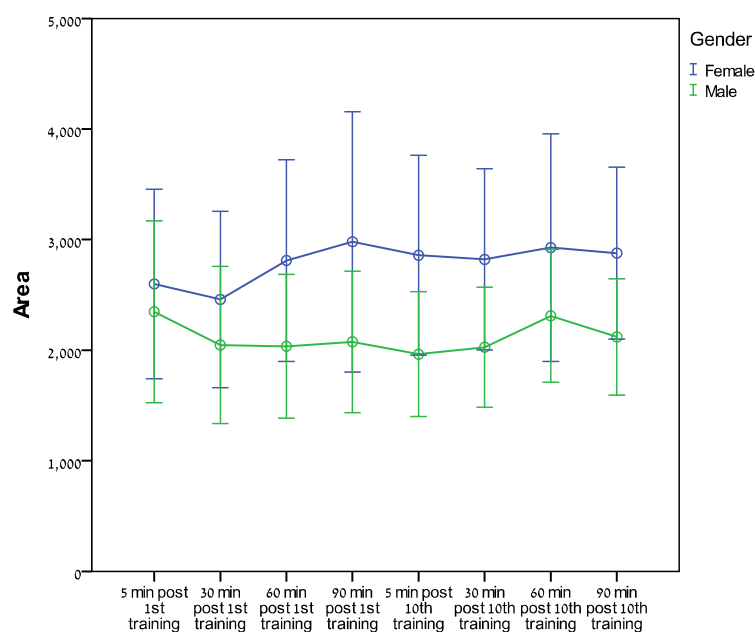


Figure 6.10 Volitional swallowing MEP area ($\mu V \cdot ms$): means and confidence intervals at 5, 30, 60 and 90 min post 1st training session, and 5, 30, 60 and 90 min post 10th training session, by gender.

6.1.1.3.3 *Summary: Immediate changes: 1st session vs. 10th session*

Examination of the differences in MEP area between the data that was acquired immediately after the first training session and the data acquired immediately after the last training session revealed no changes over time and no interaction of TIME*TRAINING.

In the volitional contraction task, there was a significant effect of AGE, with Older subjects having a larger MEP area than Young subjects. In the volitional swallowing task, there was a marginally significant effect of GENDER, with Females having a larger MEP area than Males.

6.1.1.4 *Cumulative changes – 2-week training*

6.1.1.4.1 *Submental muscle MEPs during volitional contraction*

Factorial ANOVA examined the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (contraction MEP area) between baseline measures and post 2-week training measures (post-training *minus* baseline) (SKL: 8 young and 6 old, 8 female and 6 male; STR: 7 young and 7 old, 8 female and 6 male). There were no significant effects (Table 6.5 p. 186). There was a marginally significant main effect of TRAINING ($F(1, 22) = 3.62, p = 0.07$, Cohen's $d = 0.79$). Figure 6.11 presents the results by training group. Examination of the data indicate that although the effect of TRAINING did not reach significance, there was a trend towards a difference between the two groups, with STR having an increase in MEP area and SKL having a decrease following training. In the STR group ($n = 14$) there was an estimated increase of $729 \mu V \cdot ms$ from baseline to post testing ($SD 1602$; CI for the difference $[-148, 1607]$, Cohen's $d = 0.49, t(13) = 1.73, p = 0.11$). In SKL group ($n = 14$) there was an estimated decrease of $414 \mu V \cdot ms$ from baseline to post testing ($SD 1398$; CI for the difference $[-1298, 469]$, Cohen's $d = 0.27, t(13) = 1.05, p = 0.31$). The effect of AGE was not significant (Cohen's $d = 0.51$). Figure 6.12 presents the results by age group.

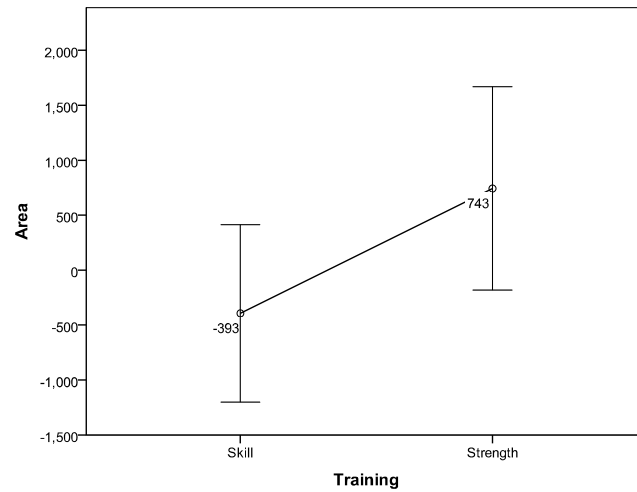


Figure 6.11 Contraction MEP area ($\mu V \cdot ms$): mean difference between baseline and post 2-week training (outcome minus baseline) and 95% confidence intervals, by training group.

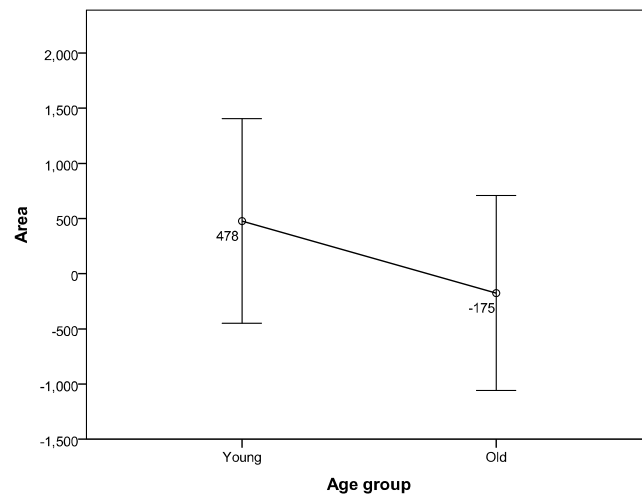


Figure 6.12 Contraction MEP area ($\mu V \cdot ms$): mean difference between baseline and post 2-week training (outcome minus baseline) and 95% confidence intervals, by age group.

A non-parametric comparison was conducted to explore the difference between SKL-I and SKL-D in MEP magnitude (calculated as MEP area at post 2 weeks *minus* baseline). Mann-Whitney test for independent samples was used with the SKL-I vs. SKL-D as the independent variable and the difference in MEP size as the dependent variable. There was no significant difference between SKL subgroups ($U = 18.00$, $z = -0.77$, $p = 0.44$).

6.1.1.4.2 Submental muscle MEPs during volitional swallowing

Four-factor ANOVA with TIME (baseline vs. post 2 weeks), TRAINING (SKL vs. STR), GENDER, and AGE was conducted (SKL: 8 young and 5 old, 8 female and 5 male; STR: 6 young and 6 old, 7 female and 5 male). There were no significant effects (Table 6.5 p. 186).

Figure 6.13 presents the difference between baseline and post-training in swallowing MEP area, by training group ($p = 0.29$, Cohen's d for the effect of TRAINING = 0.49). For STR Cohen's d for the effect of training in STR = 0.27; for SKL = 0.19. The effect of AGE (Figure 6.14) was not significant (Cohen's $d = 0.36$).

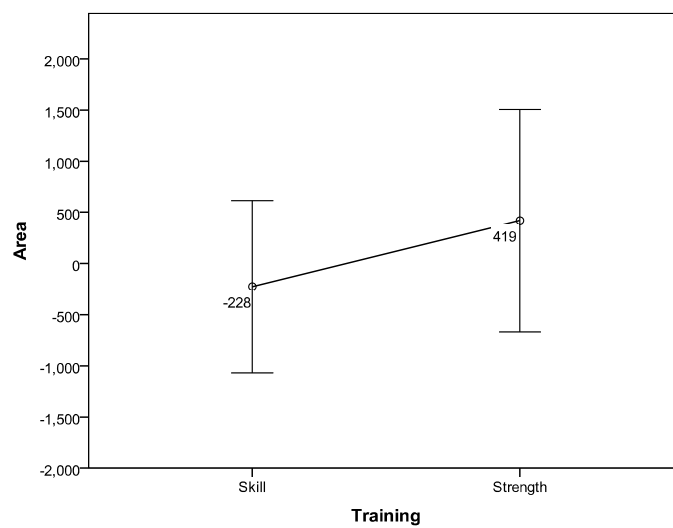


Figure 6.13 Swallowing MEP area ($\mu V \cdot ms$): mean difference between baseline and post 2-week training (outcome minus baseline) and 95% confidence intervals, by training group.

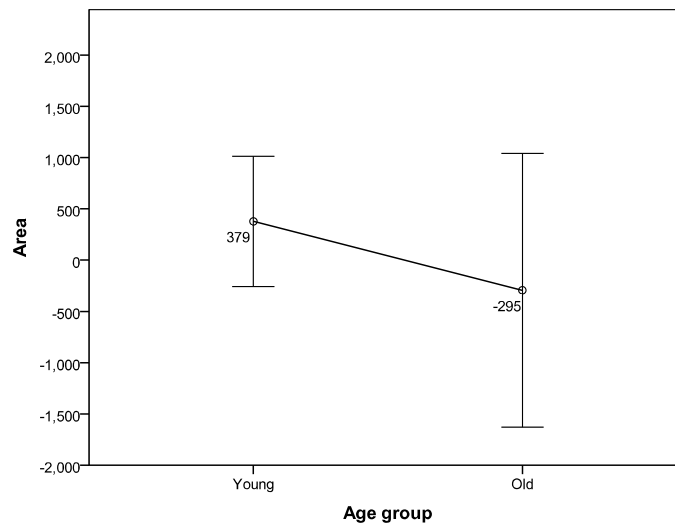


Figure 6.14 Swallowing MEP area ($\mu V \cdot ms$): mean difference between baseline and post 2-week training (outcome minus baseline) and 95% confidence intervals, by age group.

A non-parametric analysis was conducted to explore the difference between SKL-I and SKL-D in MEP magnitude (calculated as MEP at post 2 weeks *minus* baseline). Mann-Whitney test for independent samples was used with the SKL-I and SKL-D as the independent variable and the difference in MEP size as the dependent variable. There was no significant difference between SKL subgroups ($U = 19.00$, $z = -0.14$, $p = 0.88$).

6.1.1.4.3 Summary: Cumulative changes – 2-week training

To summarize, when examining the changes in MEP area following training, there were no significant differences between training groups. However, visual examination of the data indicates that although the effect of training type did not reach significance, there was a trend towards a difference in the changes in submental contraction MEP following training, with subjects in STR training having a non-significant increase in MEP area and subjects in SKL training having a non-significant decrease following training.

Table 6.5 Factor effects (F , df , p values): Training group (SKL v. STR), gender, and age group (Old vs. Young): MEP area (significant results are in bold)

Measure	Task	Factors, F (df), p value
Immediate changes post 1 st	Submental muscle MEPs during volitional	Within-group effects:
		TIME $F(1.89, 35.97) = 0.19$, $p = 0.81$
		TIME*TRAINING $F(1.89, 35.97) = 1.32$, $p = 0.28$
		TIME*AGE*TRAINING $F(1.89, 35.97) = 1.43$, $p = 0.25$

training session	contraction	<p>TIME*GENDER*TRAINING $F(1.89, 35.97) = 0.19, p = 0.81$</p> <p>TIME*TRAINING*AGE*GENDER $F(1.89, 35.97) = 0.06, p = 0.93$</p> <p>Between groups effects:</p> <p>TRAINING $F(1, 19) = 1.24, p = 0.28$</p> <p>GENDER $F(1, 19) = 0.98, p = 0.33$</p> <p>AGE $F(1, 19) = 4.27, p = 0.053$</p>
	Submental muscle MEPs during volitional swallowing	<p>Within-groups effects:</p> <p>TIME $F(2.57, 41.26) = 0.58, p = 0.60$</p> <p>TIME*TRAINING $F(2.57, 41.26) = 0.36, p = 0.75$</p> <p>TIME*AGE*TRAINING $F(2.57, 41.26) = 1.82, p = 0.16$</p> <p>TIME*GENDER*TRAINING $F(2.57, 41.26) = 1.06, p = 0.37$</p> <p>TIME*TRAINING*AGE*GENDER $F(2.57, 41.26) = 0.46, p = 0.68$</p> <p>Between-groups effects:</p> <p>TRAINING $F(1, 16) = 0.11, p = 0.75$</p> <p>GENDER $F(1, 16) = 2.20, p = 0.16$</p> <p>AGE $F(1, 16) = 2.12, p = 0.17$</p>
Immediate changes post 10 th training session	Submental muscle MEPs during volitional contraction	<p>Within-groups effects:</p> <p>TIME $(F(1.49, 28.45) = 0.43, p = 0.59$</p> <p>TIME*TRAINING $F(1.49, 28.45) = 1.79, p = 0.19$</p> <p>TIME*AGE*TRAINING $F(1.49, 28.45) = 0.86, p = 0.40$</p> <p>TIME*GENDER*TRAINING $F(1.49, 28.45) = 0.42, p = 0.60$</p> <p>TIME*TRAINING*AGE*GENDER $F(1.49, 28.45) = 0.08, p = 0.86$</p> <p>Between-groups effects:</p> <p>TRAINING $F(1, 19) = 3.11, p = 0.09$</p> <p>GENDER $F(1, 19) = 2.16, p = 0.16$</p> <p>AGE $F(1, 19) = 9.46, p = 0.006$</p>
	Submental muscle MEPs during volitional swallowing	<p>Within-groups effects:</p> <p>TIME $F(2.24, 35.96) = 0.63, p = 0.55$</p> <p>TIME*TRAINING $F(2.24, 35.96) = 0.24, p = 0.81$</p> <p>TIME*TRAINING*AGE $F(2.24, 35.96) = 0.84, p = 0.45$</p> <p>TIME*GENDER*TRAINING $F(2.24, 35.96) = 0.90, p = 0.43$</p> <p>TIME*TRAINING*AGE*GENDER $F(2.24, 35.96) = 0.77, p = 0.48$</p> <p>Between-groups effects:</p> <p>TRAINING $F(1, 16) = 0.16, p = 0.69$</p> <p>GENDER $F(1, 16) = 5.16, p = 0.037$</p> <p>AGE $F(1, 16) = 5.26, p = 0.036$</p>
Immediate changes: 1 st session vs.	Submental muscle MEPs during volitional	<p>Within-groups effects:</p> <p>TIME $F(3.32, 59.9) = 0.74, p = 0.54$</p> <p>TIME*TRAINING $F(3.32, 59.9) = 0.68, p = 0.58$</p>

10 th session	contraction	<p>TIME*TRAINING*AGE $F(3.32, 59.9) = 1.47, p = 0.27$</p> <p>TIME*TRAINING*GENDER $F(33.32, 59.9) = 0.88, p = 0.46$</p> <p>TIME*TRAINING*AGE*GENDER $F(3.32, 59.9) = 0.67, p = 0.61$</p> <p>Between-groups effects:</p> <p>TRAINING $F(1, 18) = 2.78, p = 0.11$</p> <p>GENDER $F(1, 18) = 1.09, p = 0.31$</p> <p>AGE $F(1, 18) = 5.11, p = 0.036$</p>
	Submental muscle MEPs during volitional swallowing	<p>Within-groups effects:</p> <p>TIME $F(3.84, 61.58) = 0.89, p = 0.47$</p> <p>TIME*TRAINING $F(3.84, 61.58) = 0.31, p = 0.87$</p> <p>TIME*TRAINING*AGE $F(3.84, 61.58) = 1.25, p = 0.30$</p> <p>TIME*TRAINING*GENDER $F(3.84, 61.58) = 1.36, p = 0.26$</p> <p>TIME*TRAINING*AGE*GENDER $F(3.84, 61.58) = 0.67, p = 0.61$</p> <p>Between-groups effects:</p> <p>TRAINING $F(1, 16) = 0.19, p = 0.67$</p> <p>GENDER $F(1, 16) = 4.41, p = 0.052$</p> <p>AGE $F(1, 16) = 2.56, p = 0.13$</p>
Cumulative changes (post 2-week training)	Submental muscle MEPs during volitional contraction	<p>Between-groups effects:</p> <p>TRAINING $F(1, 22) = 3.62, p = 0.07$</p> <p>AGE $F(1, 22) = 1.48, p = 0.23$</p> <p>GENDER $F(1, 22) = 0.07, p = 0.78$</p> <p>TRAINING*AGE $F(1, 22) = 0.02, p = 0.89$</p> <p>TRAINING*GENDER $F(1, 22) = 0.34, p = 0.56$</p>
	Submental muscle MEPs during volitional swallowing	<p>Between-groups effects:</p> <p>TRAINING $F(1, 19) = 1.18, p = 0.29$</p> <p>AGE $F(1, 19) = 0.64, p = 0.43$</p> <p>GENDER $F(1, 19) = 0.35, p = 0.55$</p> <p>TRAINING*AGE $F(1, 19) = 0.60, p = 0.45$</p> <p>TRAINING*GENDER $F(1, 19) = 0.17, p = 0.68$</p>

6.1.1.5 *Summary: Neurophysiological changes – 2-week training*

Analyses of MEP measurements taken at various time points over the 2-week training period revealed significant and marginally significant effects. The data indicated that there was a marginally significant trend of subjects in STR training having an increase in MEP area in submental contraction task in comparison to subjects in SKL training who had decreased MEP area, when measured immediately after the 1st training session and at post-training.

Age and gender significantly affected MEP size. Immediately after the 10th training session, Females had significantly larger swallowing MEPs than Males, regardless of training type. Older subjects had larger MEP area than Young subjects. This effect was significant in both tasks immediately after the 10th training session, and was marginally significant in the contraction task immediately after the 1st training session.

Lastly, there were no differences between SKL subgroups in MEP area. For each of the training groups (SKL and STR), the effect size for training effects varied from very small to small effects in the swallowing task up to medium in the contraction task.

6.1.2 Four-week training

Data were available for six of the 10 participants (four did not have recordable MEPs). Of these, one had MEPs during volitional contraction but not during volitional swallowing. The rest (n = 5) had both volitional swallowing and contraction MEP (SKL-D 53 F, SKL-D 88 F, SKL-I 22 F STR 35 F, STR 22 F). Due to low number of subjects in each training groups, descriptive statistics are presented. The data is presented as percent change in MEP magnitude from baseline to the other measure taken. The results consist of a description of the trends seen in the graphs and do not imply statistically significant effects.

6.1.3 Post 18th training session

Data are presented for six participants in the volitional contraction task and five participants in the volitional swallowing task.

Submental muscle MEPs during volitional contraction

Percentage changes in MEP areas are presented in Figure 6.15. Relative to baseline measurement, at 90 min after the 18th training session, two participants had a trend towards an increase (SKL-I 22 F, STR 22 F), two had a trend towards a decrease (SKL-D 88, STR35 F), and two had no change in MEP area (SKL-D 53 F, SKL-I 67).

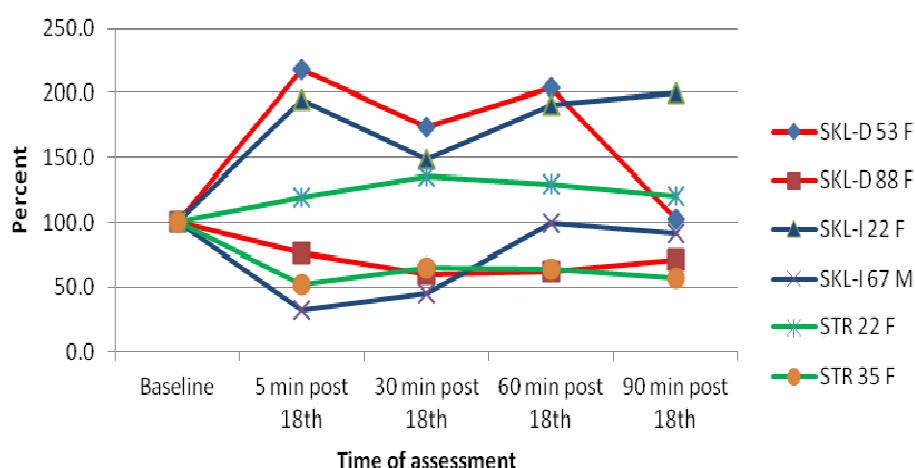


Figure 6.15 Percentage of change in mean of MEP area from baseline (100%) to 5, 30, 60 and 90 min post the 18th training session, during volitional contraction, for each participant in the 4-week protocol.

Submental muscle MEPs during volitional swallowing

Percentage change in MEP area is presented in Figure 6.16. Relative to baseline, at 90 min post 18th training session two participants had a trend towards a decrease (STR 35 F, SKL D 53 F), two had no change (SKL-I 22 F, SKL-D 88 F), and one had a trend towards an increase (STR 22 F).

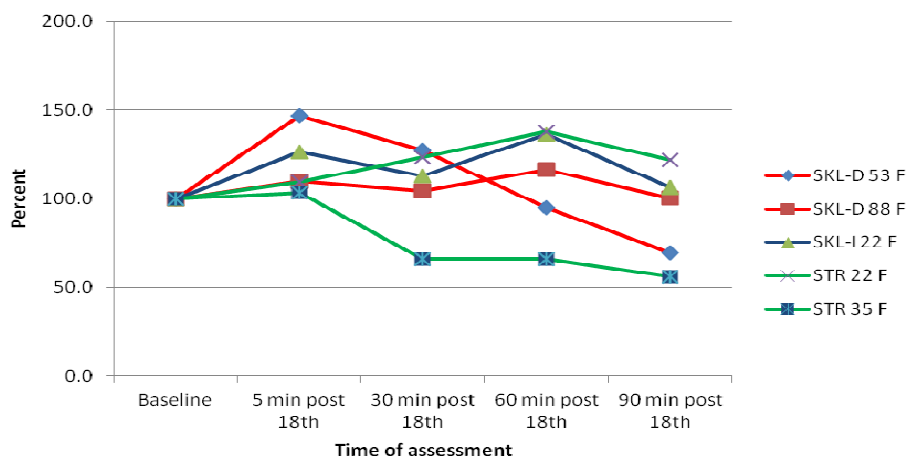


Figure 6.16 Percentage of change in mean of MEP area from baseline (100%) to 5, 30, 60 and 90 min post the 18th training session, during volitional swallowing, for each participant in the 4-week protocol.

6.1.4 Cumulative changes – 4-week training

Submental muscle MEPs during volitional contraction

Percentage change in MEP area is presented in (Figure 6.17).

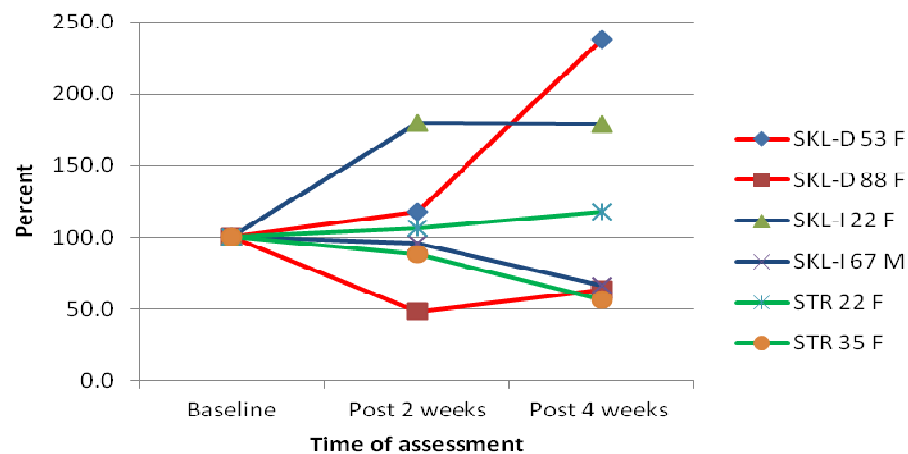


Figure 6.17 Percentage of change in mean of MEP area from baseline (100%) to post 2-week and to post 4-week training, during volitional contraction, for each participant in the 4-week protocol.

Relative to baseline measures, two subjects had a trend towards a decrease from post 2-week to post 4-week training and at 4 weeks had lower MEPs area than baseline (STR 35 F, SKL-I 67 M). One subject had no change from 2 weeks to 4 weeks post training but at both time points had greater MEP area than baseline (SKL-I 22 F). Two had a trend towards a slight increase from 2-week to 4-week measures (STR 22 F, SKL-D 88 F). One subject had an increase from baseline to post 2 weeks and from post 2 weeks to post 4 weeks (SKL-D 53 F).

Submental muscle MEPs during volitional swallowing

Percentage change in MEP area is presented in Figure 6.18.

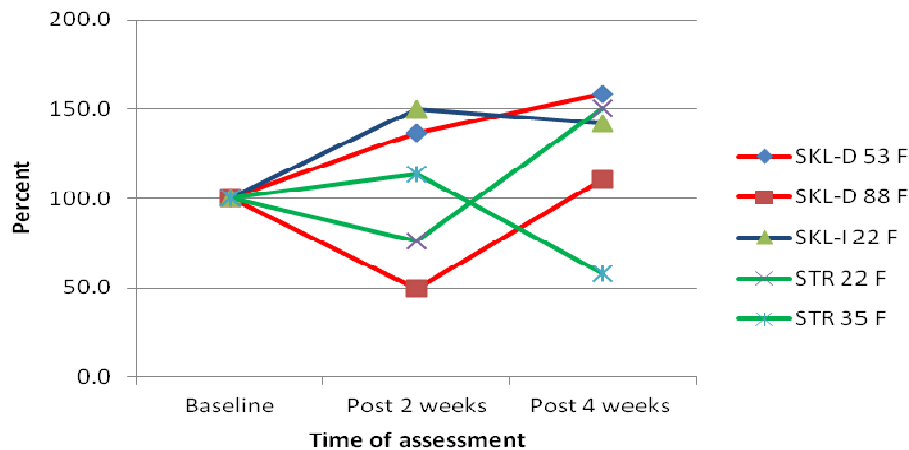


Figure 6.18 *Percentage of change in mean of MEP area from baseline (100%) to post 2 weeks and to post 4 weeks of training, during volitional swallowing, for each participant the 4-week protocol.*

Three subjects had a trend towards an increase from post 2 weeks to post 4 weeks: two had a decrease from baseline to post 2 weeks, followed by an increase from post 2 weeks to post 4 weeks, that exceeded the baseline value (SKL-D 88, STR 22 F), and one had a stable increase from baseline to post 2 weeks to post 4 weeks (SKL-D 53 F). Two subjects had a decrease from post 2 weeks to post 4 weeks: one stayed above baseline (SKL-I 22 F) and one had a decrease below baseline (STR 35 F).

6.1.5 Summary: Neurophysiological changes - Submental MEPs - 4-week training

The low number of subjects in each training group did not allow for statistical testing implementation. Therefore, descriptive statistics were used. Different subjects had different patterns of change, with some showing a trend towards an increase in MEP area during swallowing and contraction (SKL-D 53 F, SKL-I 22F) some showing an increase in MEP area during swallowing and a decrease during contraction (SKL-D 88, STR 22 F), and a decrease in swallowing and an increase in contraction (STR 35 F). No clear pattern is present.

6.2 Biomechanical changes

6.2.1 Pharyngeal pressure events

6.2.1.1 Two-week training

Manometry pressures from sensor 1 (upper pharynx), sensor 2 (mid-pharynx), and sensor 3 (UES) were available from 18/20 participants from the STR group (9 young and 9 old, 10 females and 8 males) and 18/20 participants from the SKL group (9 young and 9 old, 8 females and 10 males). SKL subgroups consisted of SKL-I (5 young and 5 old, 5 females and 5 males), and SKL-D (4 young and 4 old, 3 females and 5 males). The number of subjects included in each analysis will not be mentioned unless it is different from above. Missing data from the four participants (10% of the sample) was due to intolerance the catheter placement.

Manometry pressure from sensor 3 (UES) for the effortful saliva swallowing task was missing for one young male from SKL-D. In addition, data from sensor 3 during non-effortful water swallowing was missing for one young male from SKL-I. Missing data were due to nadir pressures that were defined as outliers (greater than 3 *SD* from the sample mean) and were removed from the analysis. To avoid confusion, the number of subjects with valid data for UES activation is reported in the text.

6.2.1.2 Peak amplitude pressure

6.2.1.2.1 Peak amplitude of the pressure event at sensor 1 (upper pharynx)

Sensor 1 (upper pharynx) peak pressure in effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 1 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.12, p. 212).

In the SKL group, the estimated mean difference was a 6.7 mmHg (*SD* 31.2, *CI* [-9.1, 22.5]) *increase* from baseline to post-training. In the STR group, the estimated mean difference was a 8.8 mmHg (*SD* 31.6, *CI* [-6.6, 24.2]) *increase* from baseline to post-training. Effect sizes are reported in Table 6.7.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 1 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.13, p. 214).

Sensor 1 (upper pharynx) peak pressure in effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 1 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.12, p. 212).

In SKL, the estimated mean difference was a 12.4 mmHg (*SD* 35.2, *CI* [-5.0, 29.8]) *increase* from baseline to post-training. In STR, the estimated mean difference was a 10.6 mmHg (*SD* 35.1, *CI* [-6.3, 27.6]) *increase* from baseline to post-training. Effect sizes are reported in Table 6.7.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 1 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.13, p. 214).

Sensor 1 (upper pharynx) peak pressure in non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 1 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.12, p. 212). The effect of GENDER*AGE was significant ($F(1, 28) = 6.08, p = 0.02, d = 0.92$). See Table 6.6 for estimated means for this interaction. Figure 6.19 displays the change from baseline to post-training (post-training *minus* baseline) for each age group in each gender. The graph reveals that while younger females and older males had little change, older females and younger males had large changes following training, in peak pressure of sensor 1 in non-effortful saliva swallowing task. Additional analyses were conducted to test if the changes in young females and older males were statistically significant, using a paired-samples t-test. In younger males, there was a marginally significant increase in pressure ($t(7) = 2.31, p = 0.054$), and in older females there was no significant change in pressure ($t(7) = 1.35, p = 0.22$). In addition, the effect of TRAINING*GENDER approached significance ($F(1, 28) = 3.47, p = 0.07, d = 0.70$) (Figure 6.20). Females in SKL, Males in STR, and Males in SKL had a trend towards an increase in peak pressure of sensor 1 in non-effortful saliva than Females in STR.

Table 6.6 Interaction of GENDER*AGE: sensor 1 (upper pharynx) peak pressure (mmHg) in non-effortful saliva swallowing task: mean difference post-training minus baseline, SD, and 95% CI for the mean difference

Gender	Age Group	Mean difference	SD	95% Confidence Interval	
				Lower Bound	Upper Bound
Female	Young	-1.2	36.6	-20.8	18.3
	Old	20.4	42.6	0.8	46.0
Male	Young	21.8	26.6	-0.05	43.7
	Old	-3.0	16.8	-24.2	15.8

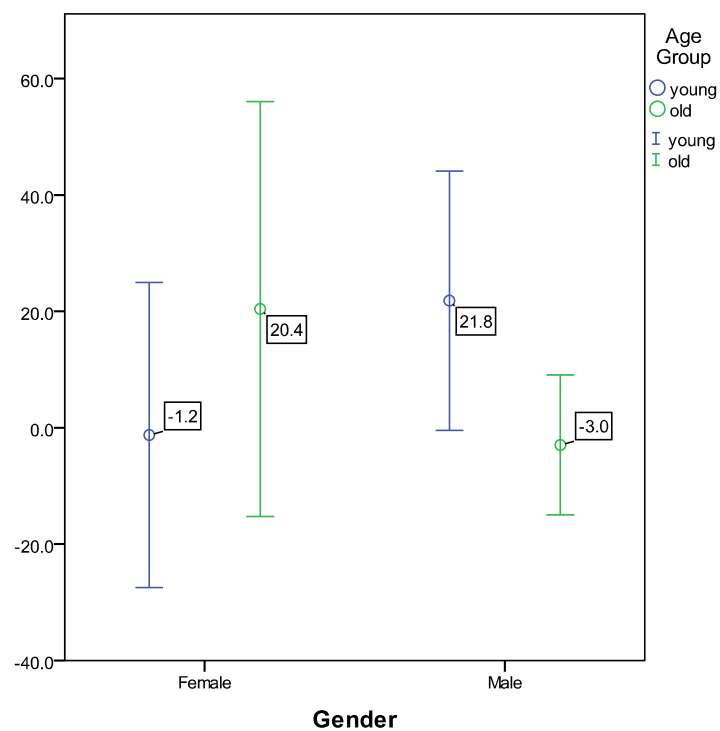


Figure 6.19 Interaction of GENDER*AGE: sensor 1 (upper pharynx) peak pressure (mmHg) in non-effortful saliva swallowing task: mean difference post-training minus baseline), by age group and gender. Error bars represent 95% CI around the mean.

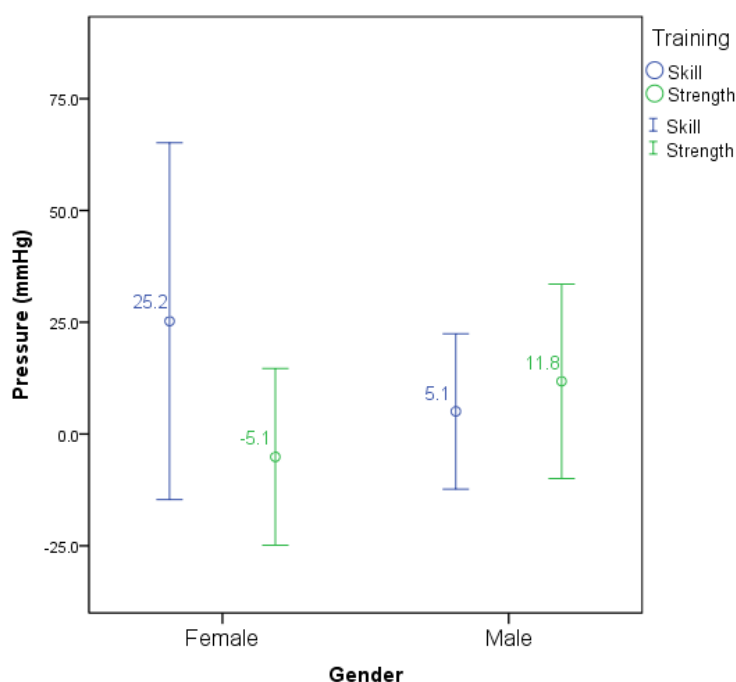


Figure 6.20 Interaction of TRAINING*GENDER: sensor 1 (upper pharynx) peak pressure (mmHg) in non-effortful saliva swallowing task: mean difference post-training minus baseline), by training group and gender. Error bars represent 95% CI around the mean.

In SKL, the estimated mean difference was a 16.6 mmHg (*SD* 36.8, *CI* [1.5, 31.6]) increase from baseline to post-training. In STR, the estimated mean difference was a 3.3 mmHg (*SD* 27.5, *CI* [-11.3, 18.0]) increase from baseline to post-training. Effect sizes are reported in Table 6.7.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 1 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.13, p.214).

Sensor 1 (upper pharynx) peak pressure in non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 1 in non-effortful 10 mL water swallowing) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.12, p. 212).

In SKL, the estimated mean difference was a 19.4 mmHg (*SD* 40.7, *CI* [1.3, 37.5]) increase from baseline to post-training. In STR, the estimated mean difference was a 1.7 mmHg (*SD* 29.5, *CI* [-15.9, 19.3]) increase from baseline to post-training. Effect sizes are reported in Table 6.7.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 1 in non-effortful 10 mL water swallowing) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.13, p.214).

Table 6.7 Effect size (Cohen's *d*) for the effect of training type (SKL *n* = 18, STR *n* = 18) on sensor 1 (upper pharynx) peak pressure

Swallowing task	SKL	STR
Effortful saliva	0.14	0.22
Effortful 10 mL water	0.23	0.31
Non-effortful saliva	0.38	0.08
Non-effortful 10 mL water	0.47	0.02

Summary: Peak amplitude of the pressure event at sensor 1 (upper pharynx)

To summarize, when comparing SKL to STR training, there was a significant interaction of GENDER*AGE in non-effortful saliva swallowing task, with older females and younger males having greater changes following training than young females and old males. Younger males had marginally significant increase and older females had no significant changes. The effect of TRAINING*GENDER approached significance in the same task, with Females in SKL, Males in STR, and Males in SKL had a trend towards an increase but Females in STR had a trend towards a decrease in pressure. Estimation for the effects sizes for each training group (Cohen's *d*) revealed that following SKL training, there were small-medium effects for non-effortful swallowing tasks and small effects for effortful tasks. Following STR training there were no effects in non-effortful tasks and small effects in effortful task.

6.2.1.2.2 Peak amplitude of the pressure events at sensor 2 (mid-pharynx)

Sensor 2 (mid-pharynx) peak pressure in effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 2 in effortful saliva swallowing) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.12, p. 212).

In SKL, the estimated mean difference was a 4.9 mmHg (SD 46.3, CI [-28.9, 19.1]) decrease from baseline to post-training. In STR, the estimated mean difference was a 14.4 mmHg (SD 41.7, CI [-37.8, 8.9]) decrease from baseline to post-training. Effect sizes are reported in Table 6.8.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 2 in effortful saliva swallowing) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.13, p.214). The effect of TRAINING was significant ($F(1, 14) = 9.17, p = 0.01$, Cohen's $d = 1.62$) (Figure 6.21). There was a mean difference of 57.2 mmHg (CI [16.7, 97.8]) between the groups. In SKL-D ($n = 8$), there was an estimated decrease of 36.7 mmHg (SD 44.8, CI [-67.1, -6.3]) from baseline to post 2-week training (Cohen's $d = 1.05$). In SKL-I ($n = 10$), there was an estimated increase of 20.5 mmHg (SD 29.8, CI [-6.3, 47.3]) from baseline to post 2-week training (Cohen's $d = 0.46$). Additional analyses were conducted to test if the change within each group was significant, using paired-samples t-test. In SKL-I there was a marginally significant increase in peak pressure ($t(9) = 2.17, p = 0.058$), and in SKL-D there was a marginally significant decrease in peak pressure ($t(7) = 2.29, p = 0.055$).

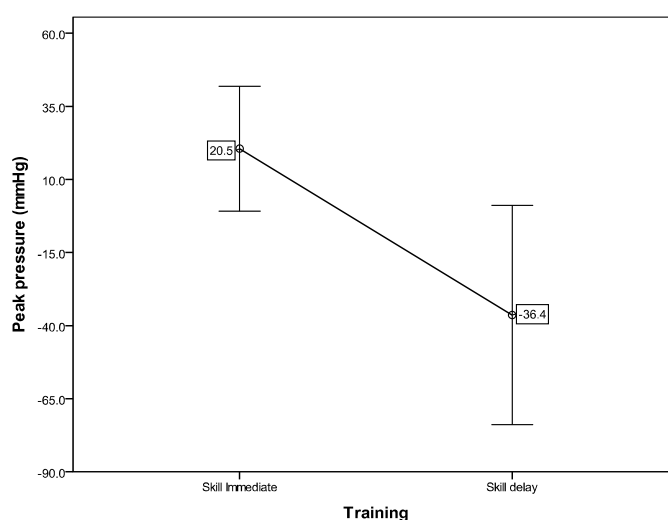


Figure 6.21 Sensor 2 (mid-pharynx) peak pressure amplitude (mmHg) in effortful saliva swallowing task: mean difference (post-training minus baseline), by training. Error bars represent 95% CI around the mean.

Since there were differences between SKL-I and SKL-D, additional analyses were carried out to examine for differences between the groups (STR $n = 18$, SKL-I $n = 10$, and SKL-D $n = 8$) over TIME. The Kruskal-Wallis non-parametric test for independent samples revealed that there are significant differences between SKL-I, SKL-D and STR in the difference in peak pressure of sensor 2 during effortful saliva swallowing task ($H(2) = 7.76, p = 0.02$), see Figure 6.22. Post hoc

analysis was carried using Mann-Whitney non-parametric test for unpaired samples. When comparing SKL-I to SKL-D ($U = 13.00$, $z = -2.39$, $p = 0.016$) and SKL-I to STR ($U = 46.00$, $z = -2.11$, $p = 0.035$), the groups were significantly different. When comparing SKL-D to STR there was no significant difference ($U = 47.00$, $z = -1.38$, $p = 0.16$). Thus, SKL-I was different from the other two groups, showing a greater increase from baseline to post training during effortful saliva swallowing.

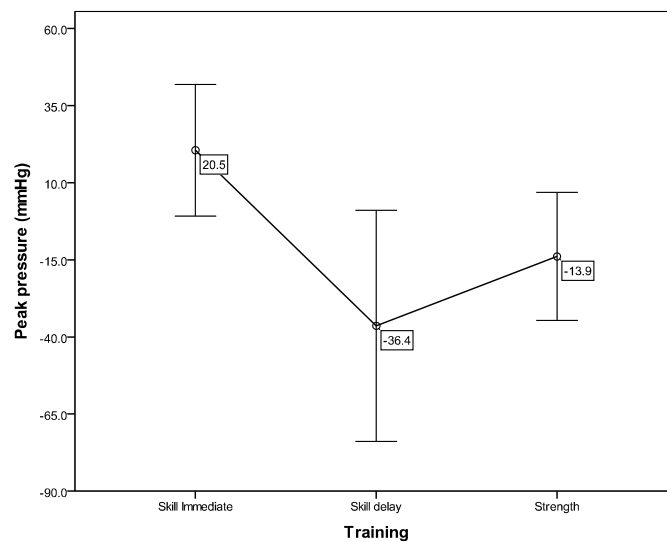


Figure 6.22 Sensor 2 (mid-pharynx) peak pressure amplitude (mmHg) in effortful saliva swallowing task: mean difference (mmHg) between baseline and post training (post-training minus baseline), by training (SKL-I, SKL-D, STR). Error bars represent 95% CI around the mean.

Sensor 2 (mid-pharynx) peak pressure in effortful 10 mL swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 2 in effortful 10 mL swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.12, p. 212).

In SKL, the estimated mean difference was a 6.3 mmHg ($SD\ 34.2$, $CI\ [-26.2, 13.6]$) *decrease* from baseline to post-training. In STR, the estimated mean difference was a 12.9 mmHg ($SD\ 42.5$, $CI\ [-6.4, 32.3]$) *increase* from baseline to post-training. Effect sizes are reported in Table 6.8.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 2 in effortful 10 mL swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.13, p.214).

The effect of TRAINING was significant ($F(1, 14) = 10.18, p = 0.01$, Cohen's $d = 1.64$) (Figure 6.23). There was a mean difference of 42.9 mmHg, between the training groups ($CI [14.0, 71.7]$). In SKL-D ($n = 8$), the estimated mean difference was a 29.7 mmHg ($SD 27.8$) decrease from baseline to post 2-week training ($CI [-51.3, -8.1]$, Cohen's $d = 1.05$). In SKL-I ($n = 10$) the estimated mean increase was of 13.2 mmHg ($SD 28.2$) increase from baseline to post 2-week training ($CI [-5.9, 32.2]$, Cohen's $d = 0.27$). Additional analyses were conducted to test the change within each group using paired-samples t-test. In SKL-I, there was no significant change ($t(9) = 1.48, p = 0.17$), but in SKL-D there was a significant decrease ($t(7) = 2.79, p = 0.03$).

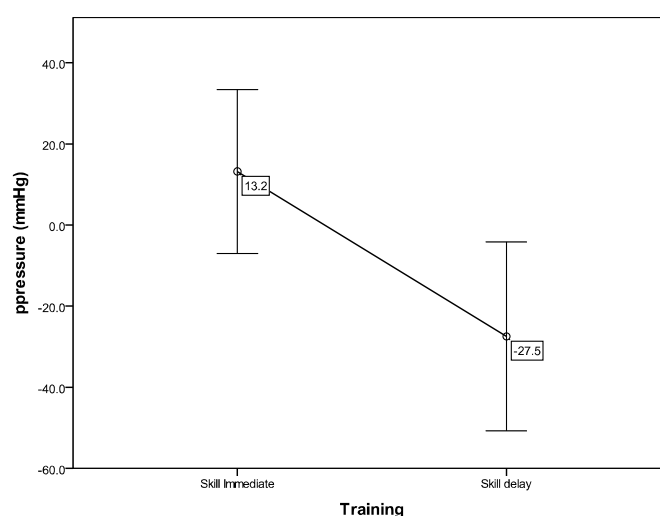


Figure 6.23 Sensor 2 (mid-pharynx) peak pressure amplitude (mmHg) in effortful 10 mL water swallowing task: mean difference (post-training minus baseline) by training. Error bars represent 95% CI around the mean.

Since there were differences between SKL-I and SKL-D, additional analyses were carried out to examine for differences between the groups over TIME. The

The Kruskal-Wallis non-parametric test for independent samples revealed significant differences between SKL-I, SKL-D and STR in the difference in peak pressure of sensor 2 during effortful 10 mL water swallowing task ($H(2) = 8.17, p = 0.017$) (see Figure 6.24). Post hoc analysis was carried using Mann-Whitney non-parametric test for unpaired samples. When comparing SKL-I to STR, the groups were not significantly different ($U = 83.00, z = -0.33, p = 0.73$). However, when comparing SKL-D to STR ($U = 26.00, z = -2.55, p = 0.01$) and SKL-D to SKL-I ($U = 11.00, z = -2.57, p = 0.01$) there were significant differences). Thus, SKL-D was different from the other two groups, showing a decrease from baseline to post training during effortful saliva swallowing.

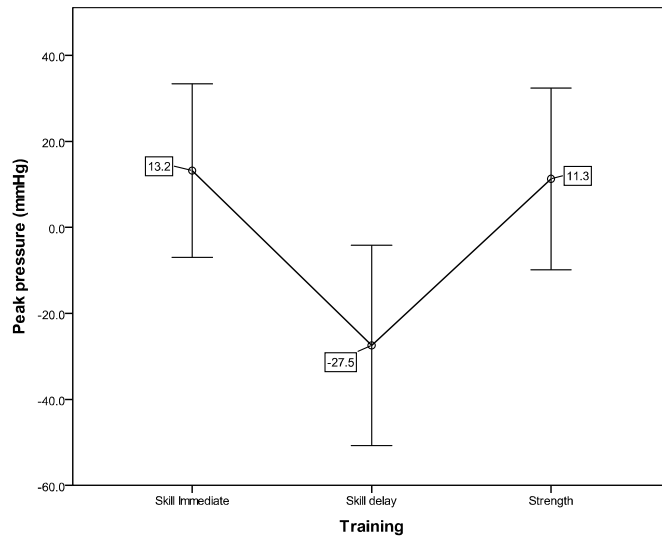


Figure 6.24 Sensor 2 (mid-pharynx) peak pressure amplitude (mmHg) in effortful 10 mL water swallowing task: mean difference post-training minus baseline), by training (SKL-I, SKL-D, STR). Error bars represent 95% CI around the mean.

Sensor 2 (mid-pharynx) peak pressure amplitude in non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 2 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no main significant effects (Table 6.12, p. 212).

In SKL, the estimated mean difference was a 7.2 mmHg (*SD* 41.3, *CI* [-33.5, 19.2]) *decrease* from baseline to post-training. In STR, the estimated mean difference was a 9.3 mmHg (*SD* 56.6, *CI* [-16.3, 35.0]) *increase* from baseline to post-training. Effect sizes are reported in Table 6.8.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 2 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.13, p.214).

There was a significant effect of TRAINING ($F(1, 14) = 4.91, p = 0.044$, Cohen's $d = 1.01$) (Figure 6.25). The mean difference between the groups was 39.1 mmHg (*CI* [1.2, 77.1]). A paired-samples t-tests was conducted for each subgroup. In SKL-I, there was a non-significant increase of 8.6 mmHg (*SD* 29.7, *CI* [-12.7, 29.8], Cohen's $d = 0.25, t(7) = 1.61, p = 0.15$). For SKL-D there was a non-significant decrease of 26.8 mmHg (*SD* 47.0, *CI* [-66.2, 12.4], Cohen's $d = 0.79, t(9) = 0.91, p = 0.38$).

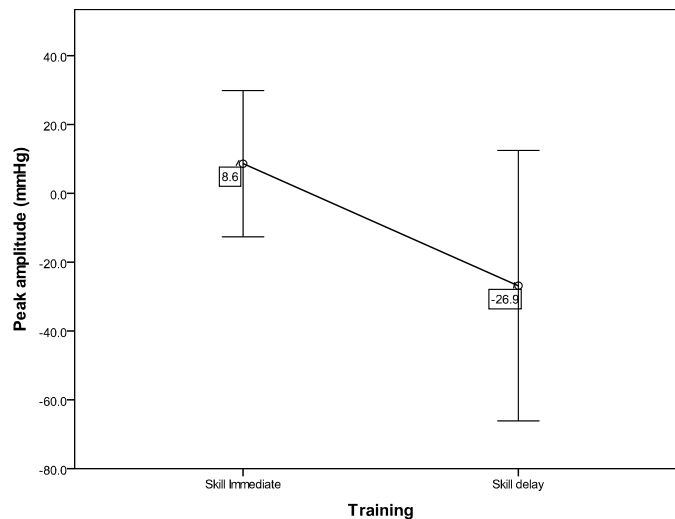


Figure 6.25 Sensor 2 (mid-pharynx) peak pressure amplitude (mmHg) in non-effortful saliva swallowing task: mean difference (post-training minus baseline), by training (SKL-I, SKL-D). Error bars represent 95% CI around the mean.

Non-parametric test for independent samples (Kruskal-Wallis) was conducted to test for differences between STR, SKL-I and SKL-D in the difference in peak 2 pressure between baseline to post 2-week training (post 2 weeks *minus* baseline). There was no significant effect of TRAINING ($H(2) = 3.74, p = 0.83$).

Sensor 2 (mid-pharynx) peak pressure amplitude in non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 2 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.12, p. 212).

In SKL, the estimated mean difference was a 10.8 mmHg ($SD\ 59.5, CI\ [-35.8, 14.3]$) *decrease* from baseline to post-training. In STR, the estimated mean difference was a 7.9 mmHg ($SD\ 31.3, CI\ [-16.5, 32.3]$) *increase* from baseline to post-training. Effect sizes are reported in Table 6.8.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (peak pressure of sensor 2 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.13, p. 214). There was a significant effect of TRAINING ($F(1, 14) = 6.26, p = 0.025$, Cohen's $d = 1.22$) (Figure 6.26) with a difference of 64.9 mmHg ($CI\ [-120.5, -9.2]$) between the groups. Paired-samples t-test was conducted for each subgroup. For the SKL-I group there was a non-significant increase of 19.4 mmHg from baseline

to post training (SD 55.9, CI [-20.6, 59.4], Cohen's $d = 0.49$, $t(9) = 1.01$, $p = 0.30$). For SKL-D there was a significant decrease of 42.9 mmHg from baseline to post training (SD 45.4, CI [-81.2, -4.5], Cohen's $d = 1.20$, $t(7) = 2.64$, $p = 0.03$).

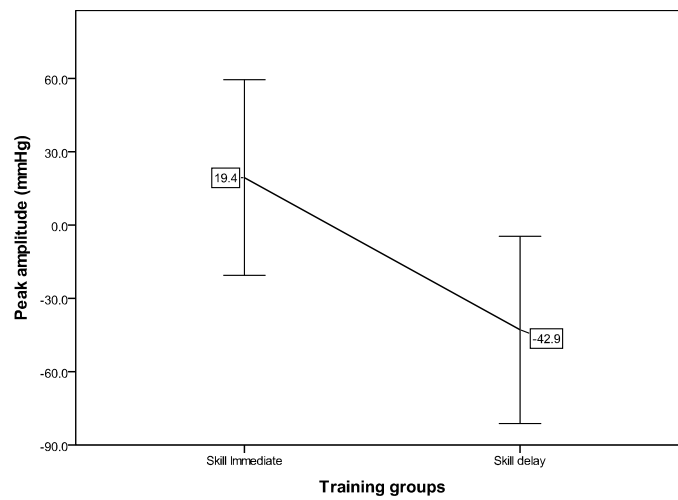


Figure 6.26 Sensor 2 (mid-pharynx) peak pressure amplitude (mmHg) in non-effortful 10 mL water swallowing task: mean difference (mmHg) between baseline and post training (post-training minus baseline), by training (SKL-I and SKL-D).

Non-parametric test for independent samples (Kruskal-Wallis) was conducted to test for differences between STR, SKL-I and SKL-D in the difference in peak 2 pressure between baseline to post 2-week training (post 2 weeks *minus* baseline). There was a marginally significant effect of TRAINING ($H(2) = 5.96$, $p = 0.051$) (Figure 6.27).

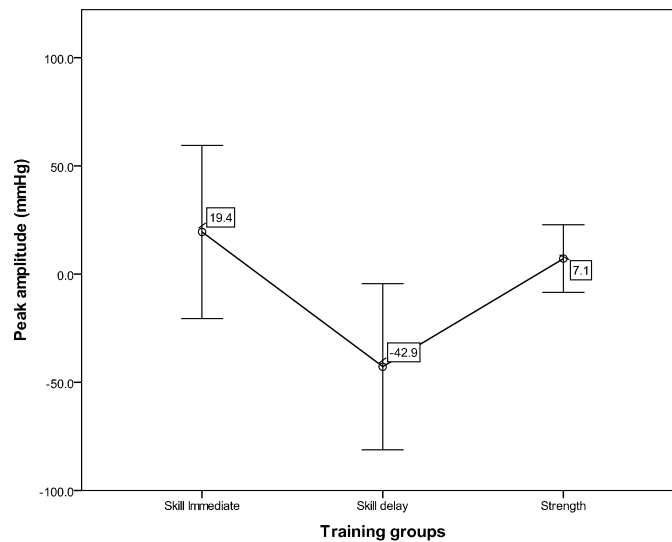


Figure 6.27 Sensor 2 (mid-pharynx) peak pressure amplitude (mmHg) in non-effortful 10 mL water swallowing task: mean difference (post-training minus baseline), by training (SKL-I, SKL-D, and STR).

Table 6.8 Effect size (Cohen's *d*) for the effect of training type (SKL *n* = 18, STR *n* = 18) on sensor 2 (mid-pharynx) peak pressure

Swallowing task	SKL	STR
Effortful saliva	0.10	0.23
Effortful 10 mL water	0.10	0.26
Non-effortful saliva	0.15	0.16
Non-effortful 10 mL water	0.19	0.16

Summary: Peak amplitude of the pressure events at sensor 2 (mid-pharynx)

To summarize, there were no differences between SKL and STR in the changes in sensor 2 peak pressure following training. Cohen's *d* effect sizes range from no effects to small effects. There was a significant difference between SKL-I and SKL-D in the change in sensor 2 peak pressure following training in all swallowing tasks (effortful and non-effortful). SKL-D group had a significant decrease in peak pressure for effortful 10 mL water swallowing and non-effortful 10 mL water swallowing tasks, and marginally significant increase for effortful saliva swallowing task. SKL-I had a marginally significant increase in effortful saliva swallowing task.

During effortful saliva swallowing task, SKL-I training was significantly different from the other two groups (SKL-D and STR) having a greater increase from baseline to outcome, while SKL-D and STR had a non-significant trend towards decrease in peak pressure. During effortful water

swallowing, SKL-D had a significant decrease in peak amplitude, while SKL-I and STR had a non-significant trends towards an increase.

6.2.1.2.3 *Nadir pressure events at sensor 3 (UES)*

To clarify, an increase in nadir pressure or decrease in UES pressure means more negativity (e.g., change from -8.0 mmHg to -10.0 mmHg). A decrease in nadir pressure or increase in UES pressure means less negativity (e.g., change from -10.0 mmHg to -8.0 mmHg).

Sensor 3 (UES) nadir pressure in effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (nadir pressure of sensor 3 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). (SKL $n = 17$, 9 old and 8 young, 8 females and 9 males; STR $n = 18$, 9 old and 9 young, 10 females and 8 males). There were no significant effects (Table 6.12, p. 212)

In the SKL group, the estimated mean difference was a 1.5 mmHg ($SD\ 7.8$, $CI\ [-3.5, 6.6]$) *increase* in UES pressure from baseline to post-training. In STR, the mean difference was a 1.3 mmHg ($SD\ 11.1$, $CI\ [-6.1, 3.4]$) *decrease* in UES pressure from baseline to post-training. Effect sizes are reported in Table 6.11.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (nadir pressure of sensor 3 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). (SKL-I $n = 10$, 5 females and 5 males, 5 old and 5 young; SKL-D $n = 7$, 3 females and 4 males, 4 old and 3 young). There were no significant effects (Table 6.13, p. 214). There was a marginally significant effect of AGE ($F(1, 13) = 3.48$, $p = 0.085$, Cohen's $d = 1.01$) with Younger subjects increasing UES pressure and Older decreasing the UES pressure following both types of SKL training (Figure 6.28)

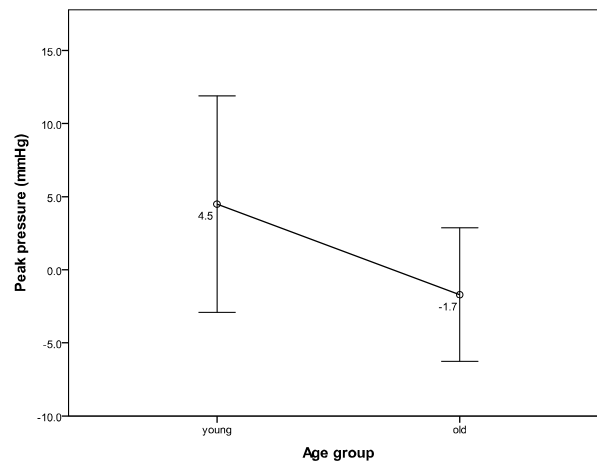


Figure 6.28 Sensor 3 (UES) nadir pressure amplitude (mmHg) in effortful saliva swallowing task: mean difference (post-training minus baseline) and 95% CI around the mean, by age (in SKL).

Sensor 3 (UES) nadir pressure in effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (nadir pressure of sensor 3 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). (SKL $n = 18$, 9 old and 9 young, 8 females and 10 males; STR $n = 18$, 9 old and 9 young, 10 females and 8 males). There were no significant effects (Table 6.12, p. 212).

In SKL, the mean difference was a 1.4 mmHg ($SD\ 7.4$, $CI\ [-6.0, 3.1]$) *decrease* in UES pressure from baseline to post-training. In STR, the mean difference was a 0.3 mmHg ($SD\ 9.7$, $CI\ [-4.2, 4.7]$) *decrease* in UES pressure from baseline to post-training. Effect sizes are reported in Table 6.11.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (nadir pressure of sensor 3 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). (SKL-I $n = 10$, 5 females and 5 males, 5 old and 5 young; SKL-D $n = 8$, 3 females and 5 males, 4 old and 4 young). There were no significant main effects (Table 6.13, p. 214).

Sensor 3 (UES) nadir pressure in non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (nadir pressure of sensor 3 in

non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). (SKL n = 18, 9 old and 9 young, 8 females and 10 males; STR n = 18, 9 old and 9 young, 10 females and 8 males) (Table 6.12, p. 212).

The main effect of GENDER was significant ($F(1, 28) = 6.64, p = 0.017$, Cohen's $d = 0.96$) (Figure 6.29). The mean difference between the genders was 4.1 mmHg (M > F) ($CI [0.8, 7.3]$). Since a difference in the change following training was found between genders, post hoc analysis was conducted to estimate the effects of training in each gender separately, using paired-samples t-test. Females had a significant *decrease* in UES pressure with a mean difference of 2.8 mmHg ($CI [0.5, 5.0]$, baseline: -9.8 mmHg ($SD 5.4$), outcome: -12.5 ($SD 6.2$), $t(17) = 2.6, p = 0.02$). Males had no change in UES pressure (mean difference 1.68 mmHg, $CI [-4.1, 0.7]$, baseline: -7.1 mmHg ($SD 1.3$), outcome: -5.4 ($SD 6.9$), $t(17) = 1.45, p = 0.17$).

Since Females had a significant decrease in UES pressure, an additional analysis was conducted to assess for differences in UES nadir between Females in STR versus Females in SKL. Females in SKL had a non-significant change in UES pressure with a mean change of 2.5 mmHg *decrease* in UES pressure ($CI [-1.1, 6.1]$, $t(7) = 1.64, p = 0.14$). Females in STR had a marginally significant *decrease* in UES pressure with a mean difference of 3.0 mmHg ($CI [-0.5, 6.5]$, $t(9) = 1.91, p = 0.08$).

Although Males did not have a significant change in UES nadir, the findings presented in 6.2.2.1 regarding reduced hyoid movement in Males following SKL training, warranted investigation of the effects of training on UES nadir. Males in SKL training had a marginally significant *increase* in UES pressure with a mean difference of 2.9 mmHg ($CI [-6.1, 0.3]$, $t(9) = 2.06, p = 0.07$).

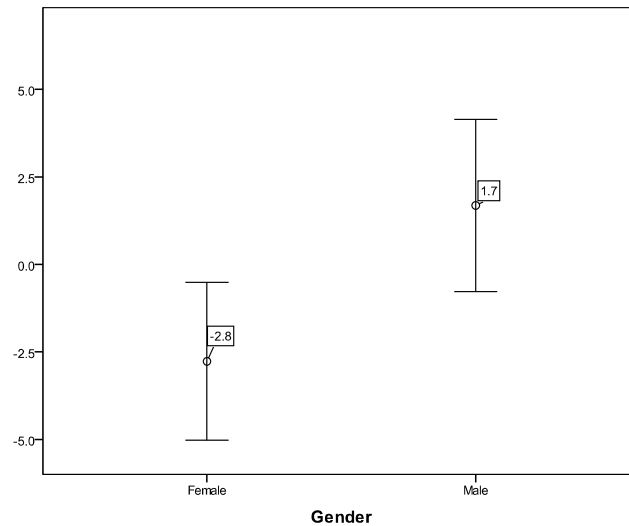


Figure 6.29 Sensor 3 (UES) nadir pressure (mmHg): mean difference (post 2-week training minus baseline) and 95% CI for the mean difference: the effect of GENDER in non-effortful saliva swallowing task.

In SKL, the estimated mean change was a 0.1 mmHg (SD 5.1, CI [-2.2, 2.5]) increase in UES pressure from baseline to post-training. In STR, the mean change was a 1.4 mmHg (SD 5.2, CI [-3.6, 0.9]) decrease in UES pressure from baseline to post-training. Effect sizes are reported in Table 6.11.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (nadir pressure of sensor 3 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value minus baseline value) (SKL-I $n = 10$, 5 females and 5 males, 5 old and 5 young; SKL-D $n = 8$, 3 females and 5 males, 4 old and 4 young) (Table 6.13, p. 214). There was a significant effect of GENDER ($F(1, 14) = 4.71$, $p = 0.048$, Cohen's $d = 1.12$) (Figure 6.30), with a difference of 4.6 mmHg between genders (CI [0.06, 9.2]). Post hoc analysis was reported above, when investigating GENDER effect in the whole group.

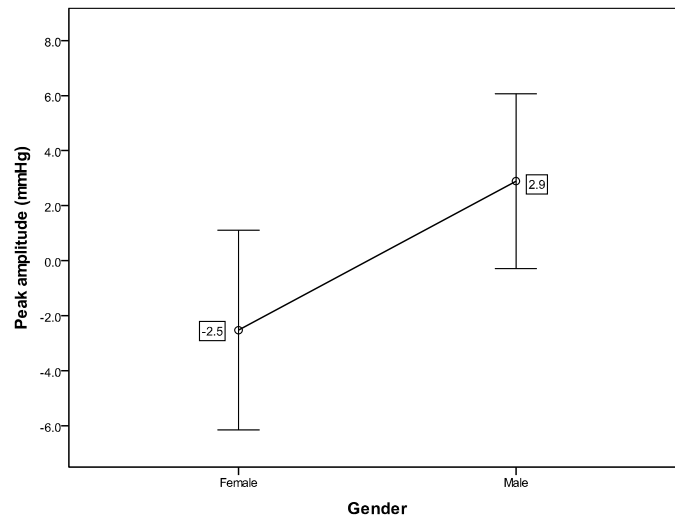


Figure 6.30 Sensor 3 (UES) nadir pressure (mmHg): mean difference (post 2 weeks minus baseline), and 95% CI for the mean difference: the effect of GENDER in non-effortful saliva swallowing task (in SKL).

Sensor 3 (UES) nadir pressure in non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (nadir pressure of sensor 3 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL $n = 17$, 9 old and 8 young, 8 females and 9 males; STR $n = 18$, 9 old and 9 young, 10 females and 8 males) (Table 6.12, p. 212).

There was a significant effect of TRAINING*GENDER ($F(1, 27) = 6.04, p = 0.02$, Cohen's $d = 0.92$) (Table 6.9 and Figure 6.31). The effect of GENDER was approaching significance ($F(1, 27) = 3.86, p = 0.060$) with a mean difference of 4.1 mmHg between genders ($CI [-8.3, 0.2]$) (Figure 6.32 and Table 6.9). The main effect of GENDER indicated that following training Females decreased UES pressure in comparison with Males (Cohen's $d = 0.79$). However, the interaction between TRAINING*GENDER revealed different effects of GENDER in each training group. Post hoc analysis for the effect of TRAINING*GENDER included analyses of the effect of GENDER in each group separately (SKL and STR), using factorial ANOVA. In SKL, GENDER had no significant effect ($F(1, 15) = 0.001, p = 0.98$). In STR, GENDER had a significant effect ($F(1, 16) = 12.17, p = 0.003$) with Females having a *decreased* UES pressure following training (mean difference: 5.1 mmHg, $CI [0.7, 9.5]$, $t(9) = 2.63, p = 0.03$, Cohen's $d = 0.86$), and Males having an *increased* UES pressure following training (mean difference: 4.1 mmHg, $CI [-8.0, 0.2]$, $t(7) = 2.46, p = 0.04$, Cohen's $d = 0.92$).

Table 6.9 Sensor 3 (UES) nadir pressure (mmHg): estimated mean difference (post-training minus baseline), 95% CI for the mean difference: interaction between TRAINING*GENDER in non-effortful 10 mL water swallowing task

Training	Gender	Mean	95% Confidence Interval	
			Lower Bound	Upper Bound
STR	Female	-5.1	-8.9	-1.2
	Male	4.1	-0.3	8.3
SKL	Female	-0.2	-4.7	4.2
	Male	-1.2	-5.7	3.1

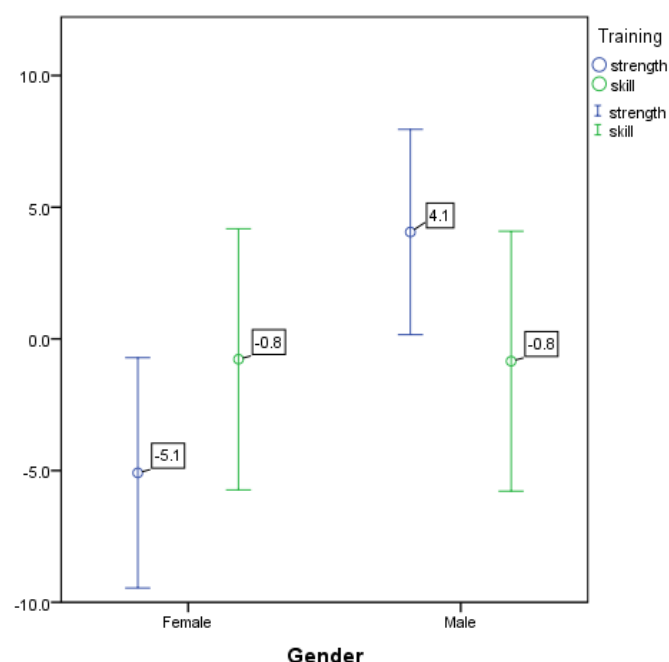


Figure 6.31 Sensor 3 (UES) nadir pressure (mmHg): mean difference in pressure between baseline and post 2-week training (post-training minus baseline) and 95% CI around the mean: interaction between TRAINING*GENDER in non-effortful 10 mL water swallowing task.

Table 6.10 Sensor 3 (UES) nadir pressure (mmHg): estimated mean difference (post-training minus baseline), 95% CI for the mean difference: the effect of GENDER in non-effortful 10 mL water swallowing task

Gender	Mean	95% Confidence Interval	
		Lower Bound	Upper Bound
Female	-2.6	-5.6	0.3
Male	1.4	-1.6	4.4

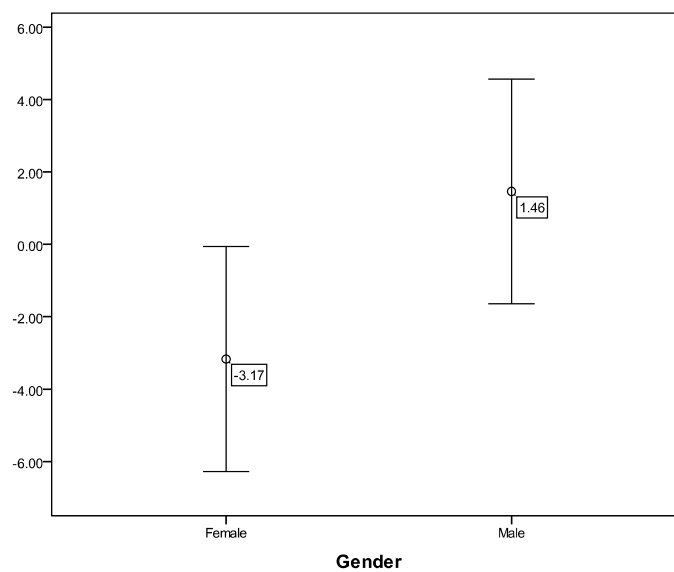


Figure 6.32 Sensor 3 (UES) nadir pressure (mmHg): mean difference (post-training minus baseline) and 95% CI around the mean: the effect of GENDER in non-effortful 10 mL water swallowing task.

In SKL, the estimated mean difference was a 0.7 mmHg (SD 6.0, CI [-3.8, 2.4]) decrease in UES pressure from baseline to post-training. In STR, the mean difference was a 0.5 mmHg (SD 7.1, CI [-3.4, 2.3]) decrease in UES pressure from baseline to post-training. Effect sizes are reported in Table 6.11

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (nadir pressure of sensor 3 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I $n = 9$, 5 females and 4 males, 5 old and 4 young; SKL-D $n = 8$, 3 females and 5 males, 4 old and 4 young). There were no significant effects (Table 6.13, p. 214).

Summary: Sensor 3 (UES) nadir pressure

In non-effortful saliva swallowing task, Females in STR had a marginally significant *decrease* in UES pressure and Males in SKL training had a marginally significant *increase* in UES pressure. In non-effortful water swallowing task, Females in STR had significantly more negativity in UES nadir pressure following training, and Males in STR had significantly less negativity in UES nadir pressure following training.

Table 6.11 Effect size (Cohen's *d*) for the effect of training type (SKL *n* = 17, STR *n* = 18) on sensor 3 (upper esophageal sphincter) nadir pressure

Swallowing task	SKL	STR
Effortful saliva	0.00	0.15
Effortful 10 mL water	0.16	0.00
Non-effortful saliva	0.07	0.27
Non-effortful 10 mL water	0.13	0.19

Table 6.12 Factor effects (*F*, *df*, *p* values): TRAINING (SKL vs. STR), GENDER, and AGE (Young vs. Old) - Manometry peak amplitude for sensor 1, 2 and 3 (significant results are in bold)

Outcome measure	Swallowing task	Factors, <i>F</i> (<i>df</i>), <i>p</i> value
Sensor 1 Peak amplitude	Effortful swallowing – saliva	TRAINING $F(1, 28) = 0.04, p = 0.84$ GENDER $F(1, 28) = 2.06, p = 0.16$ AGE $F(1, 28) = 0.01, p = 0.92$ TRAINING*GENDER $F(1, 28) = 2.71, p = 0.11$ TRAINING*AGE $F(1, 28) = 0.04, p = 0.84$ AGE*GENDER $F(1, 28) = 0.30, p = 0.58$ TRAINING*GENDER*AGE $F(1, 28) = 0.23, p = 0.63$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 28) = 0.02, p = 0.88$ GENDER $F(1, 28) = 1.08, p = 0.31$ AGE $F(1, 28) = 3.92, p = 0.057$ TRAINING*GENDER $F(1, 28) = 1.86, p = 0.18$ TIME*TRAINING*AGE $F(1, 28) = 0.04, p = 0.84$ GENDER*AGE $F(1, 28) = 0.01, p = 0.89$ GENDER*AGE*TRAINING $F(1, 28) = 0.76, p = 0.39$
	Non-effortful swallowing –	TRAINING $F(1, 28) = 1.65, p = 0.21$ GENDER $F(1, 28) = 0.05, p = 0.83$

	saliva	<p>AGE $F(1, 28) = 0.00, p = 0.95$</p> <p>TRAINING*GENDER $F(1, 28) = 3.47, p = 0.073$</p> <p>TRAINING*AGE $F(1, 28) = 0.22, p = 0.64$</p> <p>GENDER*AGE $F(1, 28) = 6.08, p = 0.02$</p> <p>TRAINING*GENDER*AGE $F(1, 28) = 1.65, p = 0.21$</p>
	Non-effortful swallowing – 10 mL water	<p>TRAINING $F(1, 28) = 2.06, p = 0.16$</p> <p>GENDER $F(1, 28) = 1.38, p = 0.25$</p> <p>AGE $F(1, 28) = 0.18, p = 0.67$</p> <p>TRAINING*GENDER $F(1, 28) = 0.97, p = 0.33$</p> <p>TRAINING*AGE $F(1, 28) = 0.19, p = 0.66$</p> <p>GENDER*AGE $F(1, 28) = 0.74, p = 0.40$</p> <p>TRAINING*GENDER*AGE $F(1, 28) = 0.62, p = 0.43$</p>
Sensor 2 - Peak amplitude	Effortful swallowing – saliva	<p>TRAINING $F(1, 28) = 0.34, p = 0.56$</p> <p>GENDER $F(1, 28) = 0.20, p = 0.66$</p> <p>AGE $F(1, 28) = 0.29, p = 0.59$</p> <p>TRAINING*GENDER $F(1, 28) = 0.02, p = 0.88$</p> <p>TRAINING*AGE $F(1, 28) = 0.03, p = 0.86$</p> <p>GENDER*AGE $F(1, 28) = 0.01, p = 0.91$</p> <p>TRAINING*GENDER*AGE $F(1, 28) = 0.01, p = 0.91$</p>
	Effortful swallowing – 10 mL water	<p>TRAINING $F(1, 28) = 2.01, p = 0.16$</p> <p>GENDER $F(1, 28) = 2.48, p = 0.12$</p> <p>AGE $F(1, 28) = 0.89, p = 0.35$</p> <p>TRAINING*GENDER $F(1, 28) = 0.43, p = 0.52$</p> <p>TRAINING*AGE $F(1, 28) = 0.03, p = 0.87$</p> <p>GENDER*AGE $F(1, 28) = 0.05, p = 0.82$</p> <p>TRAINING*GENDER*AGE $F(1, 28) = 0.05, p = 0.81$</p>
	Non-effortful swallowing – saliva	<p>TRAINING $F(1, 28) = 0.84, p = 0.36$</p> <p>GENDER $F(1, 28) = 0.08, p = 0.77$</p> <p>AGE $F(1, 28) = 0.36, p = 0.55$</p> <p>TRAINING*GENDER $F(1, 28) = 1.07, p = 0.31$</p> <p>TRAINING*AGE $F(1, 28) = 0.09, p = 0.75$</p> <p>GENDER*AGE $F(1, 28) = 0.47, p = 0.49$</p> <p>TRAINING*GENDER*AGE $F(1, 28) = 0.00, p = 0.98$</p>
	Non-effortful swallowing – 10 mL water	<p>TRAINING $F(1, 28) = 1.19, p = 0.28$</p> <p>GENDER $F(1, 28) = 0.61, p = 0.44$</p> <p>AGE $F(1, 28) = 0.38, p = 0.54$</p> <p>TRAINING*GENDER $F(1, 28) = 0.001, p = 0.97$</p> <p>TRAINING*AGE $F(1, 28) = 0.07, p = 0.78$</p> <p>GENDER*AGE $F(1, 28) = 0.06, p = 0.81$</p>

		TRAINING*GENDER*AGE $F(1, 28) = 1.50, p = 0.23$
Sensor 3 – Nadir pressure	Effortful swallowing – saliva	TRAINING $F(1, 27) = 0.71, p = 0.41$ GENDER $F(1, 27) = 2.22, p = 0.15$ AGE $F(1, 27) = 0.09, p = 0.76$ TRAINING*GENDER $F(1, 27) = 0.10, p = 0.75$ TRAINING*AGE $F(1, 27) = 3.42, p = 0.075$ GENDER*AGE $F(1, 27) = 0.09, p = 0.76$ TRAINING*AGE*GENDER $F(1, 27) = 0.03, p = 0.87$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 28) = 0.30, p = 0.58$ GENDER $F(1, 28) = 0.96, p = 0.33$ AGE $F(1, 28) = 0.01, p = 0.93$ TRAINING*GENDER $F(1, 28) = 0.63, p = 0.43$ TRAINING*AGE $F(1, 28) = 0.04, p = 0.84$ GENDER*AGE $F(1, 28) = 0.31, p = 0.58$ TRAINING*AGE*GENDER $F(1, 28) = 0.30, p = 0.59$
	Non-effortful swallowing – saliva	TRAINING $F(1, 28) = 0.91, p = 0.34$ GENDER $F(1, 28) = 6.47, p = 0.017$ AGE $F(1, 28) = 3.58, p = 0.07$ TRAINING*GENDER $F(1, 28) = 0.33, p = 0.56$ TRAINING*AGE $F(1, 28) = 0.47, p = 0.50$ GENDER*AGE $F(1, 28) = 0.94, p = 0.34$ TRAINING*AGE*GENDER $F(1, 28) = 0.35, p = 0.56$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 27) = 0.01, p = 0.91$ GENDER $F(1, 27) = 3.86, p = 0.06$ AGE $F(1, 27) = 2.03, p = 0.16$ TRAINING*GENDER $F(1, 27) = 6.04, p = 0.02$ TRAINING*AGE $F(1, 27) = 0.04, p = 0.84$ GENDER*AGE $F(1, 27) = 0.68, p = 0.41$ TIME*TRAINING*AGE*GENDER $F(1, 27) = 0.14, p = 0.71$

Table 6.13 Factor effects (F , df , p values): TRAINING (SKL-I vs. SKL-D), GENDER, and AGE (Young vs. Old): Manometry peak amplitude for sensor 1, 2 and 3 (significant results are in bold, between-group)

Outcome measure	Swallowing task	Factors, F (df), p value
Sensor 1 Peak amplitude	Effortful swallowing – saliva	TRAINING $F(1, 14) = 0.12, p = 0.74$ GENDER $F(1, 14) = 0.03, p = 0.86$

		AGE $F(1, 14) = 0.04, p = 0.85$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 0.43, p = 0.52$ GENDER $F(1, 14) = 3.03, p = 0.10$ AGE $F(1, 14) = 1.44, p = 0.25$
	Non-effortful swallowing – saliva	TRAINING $F(1, 14) = 1.15, p = 0.30$ GENDER $F(1, 14) = 1.61, p = 0.22$ AGE $F(1, 14) = 0.03, p = 0.86$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 0.75, p = 0.40$ GENDER $F(1, 14) = 1.99, p = 0.18$ AGE $F(1, 14) = 0.43, p = 0.52$
Sensor 2 - Peak amplitude	Effortful swallowing – saliva	TRAINING $F(1, 14) = 9.17, p = 0.01$ GENDER $F(1, 14) = 0.01, p = 0.90$ AGE $F(1, 14) = 0.14, p = 0.71$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 10.18, p = 0.01$ GENDER $F(1, 14) = 1.67, p = 0.22$ AGE $F(1, 14) = 0.66, p = 0.43$
	Non-effortful swallowing – saliva	TRAINING $F(1, 14) = 4.91, p = 0.044$ GENDER $F(1, 14) = 2.66, p = 0.12$ AGE $F(1, 14) = 1.13, p = 0.30$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 6.25, p = 0.025$ GENDER $F(1, 14) = 0.59, p = 0.45$ AGE $F(1, 14) = 0.05, p = 0.83$
Sensor 3 – Nadir pressure	Effortful swallowing – saliva	TIME*TRAINING $F(1, 13) = 0.44, p = 0.52$ GENDER $F(1, 13) = 1.10, p = 0.31$ AGE $F(1, 13) = 3.48, p = 0.085$
	Effortful swallowing – 10 mL water	TIME*TRAINING $F(1, 14) = 0.59, p = 0.45$ GENDER $F(1, 14) = 0.06, p = 0.81$ AGE $F(1, 14) = 0.01, p = 0.91$
	Non-effortful swallowing – saliva	TRAINING $F(1, 14) = 1.32, p = 0.27$ GENDER $F(1, 14) = 4.71, p = 0.048$ AGE $F(1, 14) = 0.97, p = 0.34$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 13) = 1.16, p = 0.30$ GENDER $F(1, 13) = 0.30, p = 0.59$ AGE $F(1, 13) = 1.41, p = 0.26$

6.2.1.3 *Pressure event durations*

6.2.1.3.1 *Duration of the pressure events at sensor 1 (upper pharynx)*

Sensor 1 (upper pharynx) duration in effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 1 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.21, p. 230).

In SKL, the estimated mean difference was of 0.011 s (*SD* 0.107, *CI* [-0.064, 0.086]) *increase* from baseline to post-training. In STR, the mean difference was of 0.053 s (*SD* 0.181, *CI* [-0.020, 0.126]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.14.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 1 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.22, p. 232).

Sensor 1 (upper pharynx) duration in effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 1 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.21, p. 230).

In SKL, the estimated mean difference was of 0.044 s (*SD* 0.082, *CI* [-0.054, 0.143]) *increase* from baseline to post-training. In STR, the mean difference was of 0.171 s (*SD* 0.252, *CI* [0.075, 0.267]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.14.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 1 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.22, p. 232).

Sensor 1 (upper pharynx) duration in non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 1 in non-

effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.21, p. 230). There was a marginally significant effect of TRAINING*AGE ($F(1, 28) = 4.11, p = 0.052$, Cohen's $d = 0.74$), with Young participants in STR having shorter duration following training and Old in STR having an increase in duration. In SKL, both Young and Old had an increase (Figure 6.33).

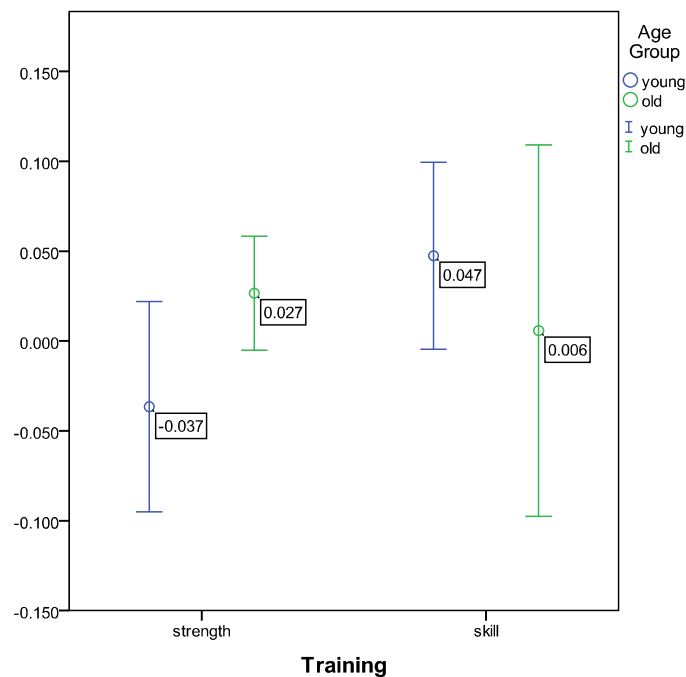


Figure 6.33 Sensor 1 (upper pharynx) duration (s): mean difference in duration (post-training minus baseline) and 95% CI around the mean: interaction of TRAINING*AGE.

In SKL, the estimated mean difference was a 0.019 s ($SD\ 0.105, CI\ [-0.025, 0.063]$) *increase* from baseline to post-training. In STR, the mean difference was a 0.007 s ($SD\ 0.067, CI\ [-0.050, 0.036]$) *decrease* from baseline to post-training. Effects sizes are reported in Table 6.14.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 1 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.22, p. 232).

Sensor 1 (upper pharynx) duration in non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 1 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.21, p. 230).

In SKL, the estimated mean difference was of 0.030 s (*SD* 0.101, *CI* [-0.015, 0.075]) *increase* from baseline to post-training. In STR, the mean difference was of 0.014 s (*SD* 0.066, *CI* [-0.030, 0.058]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.14

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 1 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.22, p. 232).

Table 6.14 Effect size (Cohen's *d*) for the effect of training type (SKL *n* = 18, STR *n* = 18): Sensor 1 (upper pharynx), pressure duration

Swallowing task	SKL	STR
Effortful saliva	0.08	0.15
Effortful 10 mL water	0.35	0.83
Non-effortful saliva	0.22	0.00
Non-effortful 10 mL water	0.34	0.13

Summary: Duration of the pressure events at sensor 1 (upper pharynx)

To summarize, there were no significant differences between SKL and STR and between SKL-I and SKL-D in the changes in sensor 1 duration. In non-effortful saliva swallowing, there was a marginally significant interaction of TRAINING*AGE, with Young subject in STR having a decrease in sensor 1 duration following training, but Old in STR and Young and Old in SKL had an increase following training.

For SKL there were small effect sizes of training. For STR there were no effects or small effect sizes of training. However, there was a larger effect size ($d = 0.83$) in effortful 10 mL water swallowing task, with a 0.17 s increase in sensor 1 duration following training.

6.2.1.3.2 Duration of the pressure events at sensor 2 (mid-pharynx)

Sensor 2 (mid-pharynx) duration in effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 2 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.21, p. 230).

In SKL, the estimated mean difference was of 0.072 s (SD 0.234, CI [-0.044, 0.187]) *increase* from baseline to post-training. In STR, the mean difference was of 0.044 s (SD 0.224, CI [-0.068, 0.157]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.15.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 2 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.22, p. 232).

Sensor 2 (mid-pharynx) duration in effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 2 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.21, p. 230). The effect of AGE was approaching significance ($F(1, 28) = 3.56$, $p = 0.07$). The mean difference between Young and Old was -0.166 s (CI [-0.014, 0.347], Cohen's $d = 0.65$) (Figure 6.34).

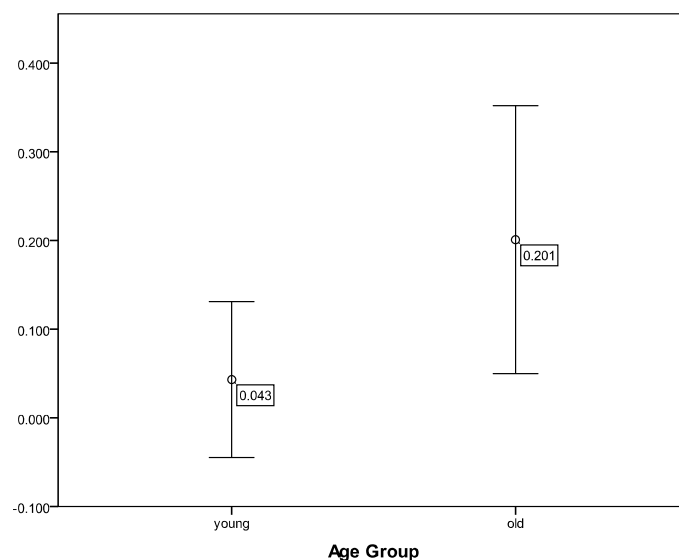


Figure 6.34 Sensor 2 duration (s) in effortful 10 mL water swallowing task. Mean difference in duration (post 2-week training minus baseline) for each age group, and 95% CI around the mean.

In SKL, the estimated mean difference was of 0.067 s (SD 0.155, CI [-0.063, 0.196]) *increase* from baseline to post-training. In STR, the mean difference was of 0.175 s (SD 0.325, CI [0.049, 0.301]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.15.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 2 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.22, p. 232).

There was a marginally significant effect of TRAINING ($F(1, 14) = 4.24, p = 0.06$, Cohen's $d = 0.97$) (Figure 6.35). SKL-I had an estimated mean difference of 0.128 s ($SD\ 0.104, CI\ [0.032, 0.224]$) increase between post training and baseline (2 weeks post *minus* baseline). SKL-D had an estimated mean difference of 0.011 s ($SD\ 0.180, CI\ [-0.120, 0.097]$) decrease between post training and baseline (2 weeks post *minus* baseline).

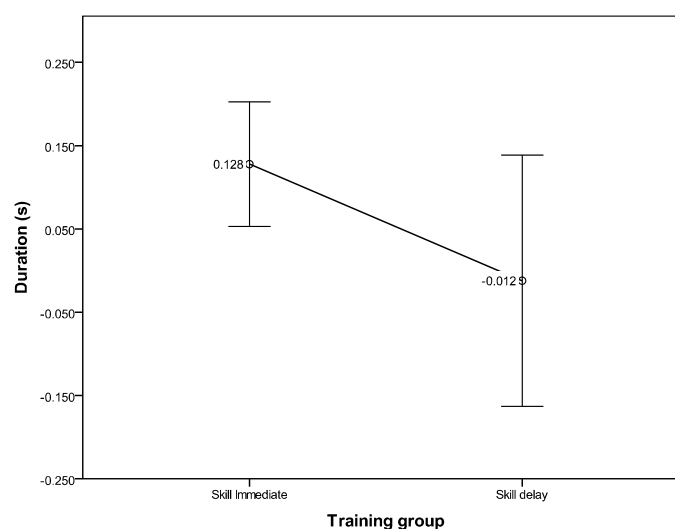


Figure 6.35 Sensor 2 duration (s) in effortful 10 mL water swallowing task. Mean difference in duration following training (post 2 weeks *minus* baseline) for each training group, and 95% CI around the mean.

Sensor 2 (mid-pharynx) duration in non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 2 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.21, p. 230).

In SKL, the estimated mean difference was of 0.055 s ($SD\ 0.108, CI\ [-0.026, 0.135]$) *increase* from baseline to post-training. In STR, the mean difference was of 0.002 s ($SD\ 0.189, CI\ [-0.076, 0.080]$) *increase* from baseline to post-training. Effects sizes are reported in Table 6.15.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 2 in non-

effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.22, p. 232).

Sensor 2 (mid-pharynx) duration in non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 2 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.21, p. 230).

In SKL, the estimated mean difference was of 0.031 s (*SD* 0.141, *CI* [-0.044, 0.107]) *increase* from baseline to post-training. In STR, the mean difference was of 0.031 s (*SD* 0.173, *CI* [-0.042, 0.105]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.15.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 2 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.22, p. 232). There was a significant effect of AGE ($F(1, 14) = 9.41, p = 0.01$) (Figure 6.36). The mean difference between the age groups was 0.174 s (*CI* [0.052, 0.295], Cohen's $d = 1.50$). Old had an estimated increase of 0.122 s (*SD* 0.113, *CI* [0.035, 0.208]) from baseline to post 2-week training, and Young had an estimated decrease of 0.052 s (*SD* 0.130, *CI* [-0.136, 0.032]) from baseline to post 2-week training. There was a marginal significant effect of GENDER ($F(1, 14) = 3.21, p = 0.095$, Cohen's $d = 0.95$) (Figure 6.37).

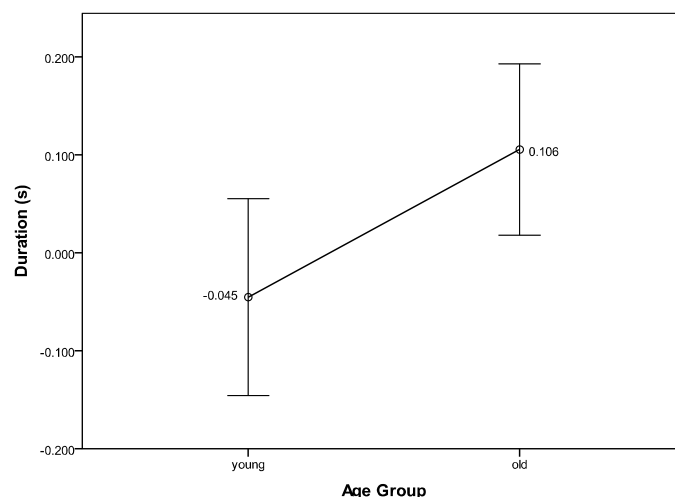


Figure 6.36 *Sensor 2 (mid-pharynx) duration (s) in non-effortful 10 mL water swallowing task: mean differences (post 2 weeks minus baseline), and 95% CI, by age group.*

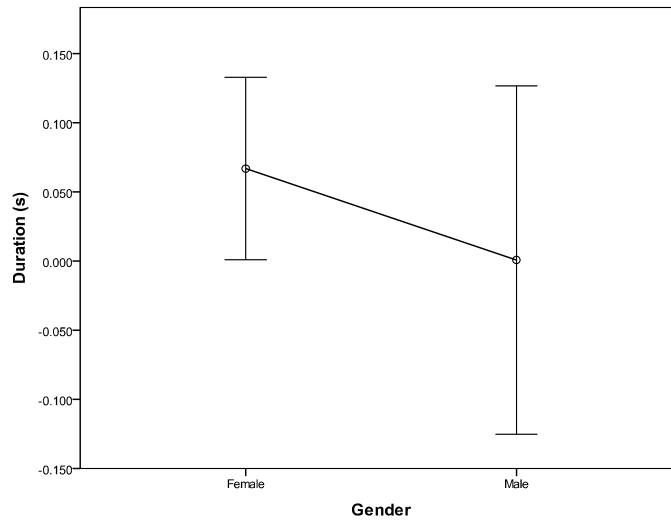


Figure 6.37 Sensor 2 (mid-pharynx) duration (s) in non-effortful 10 mL water swallowing task: mean differences (post 2 weeks minus baseline), and 95% CI, by gender.

Table 6.15 Effect size (Cohen's *d*) for the effect of training type (SKL *n* = 18, STR *n* = 18): Sensor 2 (mid-pharynx) pressure duration

Swallowing task	SKL	STR
Effortful saliva	0.27	0.13
Effortful 10 mL water	0.48	0.67
Non-effortful saliva	0.54	0.00
Non-effortful 10 mL water	0.28	0.22

Summary: Duration of the pressure events at sensor 2 (mid-pharynx)

In effortful 10 mL water swallowing, subjects receiving SKL-I produced a trend towards an increase in duration in comparison with those in SKL-D. This trend was marginally significant.

In non-effortful 10 mL water, when examining the effect of AGE in SKL subgroups, there was a significant difference between Old subjects who had a greater increase in sensor 2 duration than Young. In effortful 10 mL water swallowing, the difference between Young and Old was marginally significant in the whole cohort of subjects, with old subjects having a trend towards an increase in duration in comparison to young subjects. In addition, there was a marginally significant effect of GENDER in SKL subgroups with Females having a trend towards a larger increase in duration than Males.

For SKL training, there were small and medium effect sizes of training. For STR, there were no effect and small effect sizes of training. However, in the effortful 10 mL water task there was also a medium-large effect of TIME in STR ($d = 0.67$) with 0.17 s increase in duration at post training, similar to the effect size found for the same task in sensor 1 duration.

6.2.1.3.3 Duration of the pressure events at sensor 3 (UES)

Sensor 3 (UES) duration in effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 3 effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL $n = 17$, 9 old and 8 young, 8 females and 9 males; STR $n = 18$, 9 old and 9 young, 10 females and 8 males) (Table 6.21, p. 230). There were significant effects of TRAINING*GENDER ($F(1, 27) = 4.71, p = 0.039$, Cohen's $d = 0.82$) (Table 6.16), and TRAINING*AGE ($F(1, 27) = 4.33, p = 0.047$, Cohen's $d = 0.79$) (Table 6.17).

Females in STR and Males in SKL had a decrease in UES opening duration in effortful saliva swallowing following training, while Females in SKL and Males in STR had little change (see Figure 6.38). To further investigate this effect, a paired-samples t-test was conducted for Females in STR and Males in SKL. There was no significant change in UES opening duration in Females following STR training ($t(9) = 1.78, p = 0.11$) and no significant change in UES opening duration in Males following SKL ($t(8) = 1.25, p = 0.25$) in effortful saliva swallowing task.

The interaction of TRAINING*AGE is presented in Figure 6.39. While Old in STR had a bigger decrease in duration than Old in SKL following training (Cohen's d for the effect of training type in Old = 0.52), Young in STR had an increase in duration whereas Young in SKL had a decrease in duration (Cohen's d for the effect of training type in Young = 0.74).

Additional analyses were conducted to assess the changes in UES opening duration in effortful saliva swallowing following training in Old subjects in STR and Young in SKL, using a paired-samples t-test. For Old subjects in STR, there was no significant change in UES opening duration ($t(8) = 1.45, p = 0.19$), and for Young in SKL there was no significant change in UES opening duration ($t(7) = 1.25, p = 0.25$).

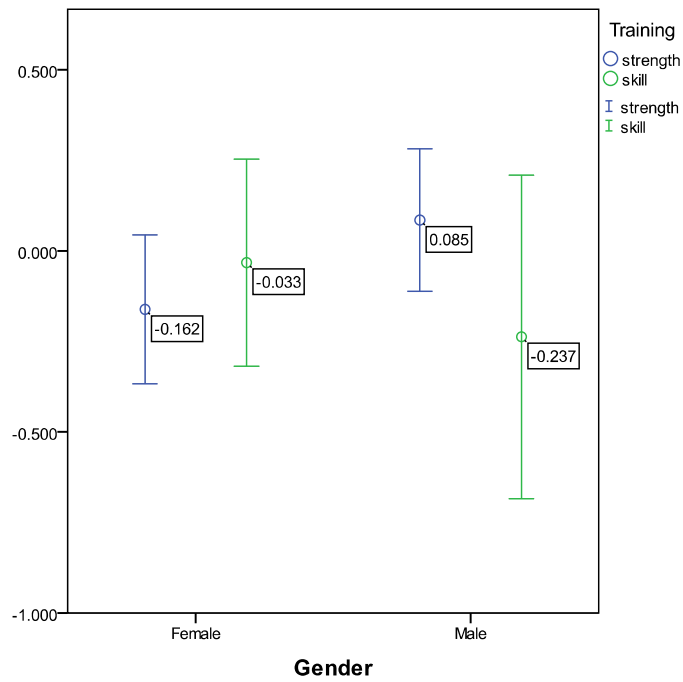


Figure 6.38 Sensor 3 (UES) duration (s) in effortful saliva swallowing tasks. Mean difference in duration (post 2-week training minus baseline) and 95% CI around the mean difference, for each training type by gender.

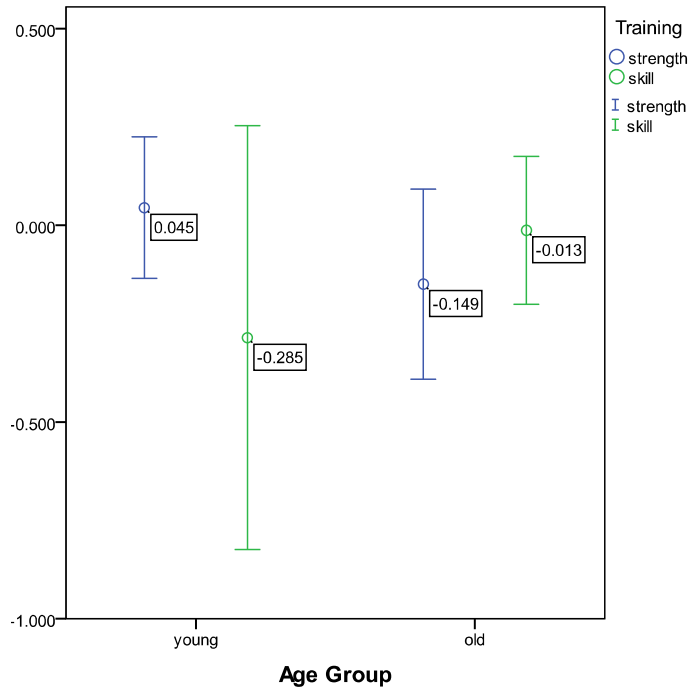


Figure 6.39 Sensor 3 (UES) duration (s) in effortful saliva swallowing tasks. Mean difference in duration (post 2-week training minus baseline) and 95% CI around the mean difference, for each training type by age group.

Table 6.16 Estimated means: interaction between TRAINING*GENDER: mean difference (post 2-week training minus baseline) in duration (s) of the pressure events at sensor 3 (UES) in effortful saliva swallowing task

Training	Gender	95% Confidence Interval		
		Mean	Lower Bound	Upper Bound
STR	Female	-0.162	-0.404	0.081
	Male	0.085	-0.186	0.356
SKL	Female	-0.014	-0.294	0.266
	Male	-0.331	-0.602	-0.060

Table 6.17 Estimated means: interaction between TRAINING*AGE: mean difference (post 2-week training minus baseline) in duration (s) of the pressure events at sensor 3 (UES) in effortful saliva swallowing task

Training	Age Group	95% Confidence Interval		
		Mean	Lower Bound	Upper Bound
STR	Young	0.054	-0.204	0.311
	Old	-0.131	-0.388	0.127
SKL	Young	-0.351	-0.631	-0.071
	Old	0.006	-0.265	0.277

In SKL, the estimated mean difference was of 0.172 s (*SD* 0.481, *CI* [-0.367, 0.022]) decrease from baseline to post-training. In STR, the mean difference was of 0.039 s (*SD* 0.286, *CI* [-0.220, 0.143]) decrease from baseline to post-training. Effects sizes are reported in Table 6.20.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 3 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value minus baseline value) (SKL-I *n* = 10, 5 old and 5 young, 5 females and 5 males; SKL-D *n* = 7, 4 old and 3 young, 3 females and 4 males). There were no significant effects (Table 6.22, p. 232)

Sensor 3 (UES) duration in effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 3 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value

minus baseline value) (SKL $n = 18$, 9 old and 9 young, 8 females and 10 males; STR $n = 18$, 9 old and 9 young, 10 females and 8 males) (Table 6.21, p. 230).

There was a significant effect of TRAINING*GENDER ($F(1, 28) = 4.99, p = 0.03$, Cohen's $d = 0.84$) (Table 6.18), and of GENDER ($F(1, 28) = 6.01, p = 0.02$, Cohen's $d = 0.90$) (Table 6.19). Figure 6.40 presents the interaction of TRAINING*GENDER. While both Females and Males demonstrated little change following STR training, following SKL training, Females and Males had opposite direction of change, with Males having decreased duration and Females having increase in sensor 3 duration. Post hoc analysis for the effect of GENDER*TRAINING included two separate factorial ANOVAs in each training group (SKL and STR) with GENDER as a factor. In STR, there was no significant effect of GENDER ($F(1,16) = 0.02, p = 0.87$) with both females and males having stable values at both time points (Cohen's d for gender effect in STR = 0.08). In SKL, there was a significant effect of GENDER ($F(1, 16) = 10.46, p = 0.005$). There was a mean difference of 0.320 s between males and females (females > males) in the difference in duration between baseline and outcome (Cohen's d for gender effect in SKL = 1.72). Additional analyses were conducted to estimate the effects of training within in gender in SKL using a paired-samples t-test. For Males in SKL, there was a significant reduction in UES opening with a mean difference of 0.198 s ($CI [-0.043, -0.354]$, baseline: 1.256 (SD 0.453), outcome: 1.057 (SD 0.382), $t(9) = 2.89, p = 0.02$). For Females in SKL, there was no significant change in UES opening duration ($t(7) = 1.74, p = 0.12$).

The effect of GENDER is graphed in Figure 6.41. Overall, regardless of training type, Males produced a decrease in duration following training, while Females produced an increased in sensor 3 duration. The mean difference between Females and Males was 0.181 s ($CI [0.031, 0.331]$).

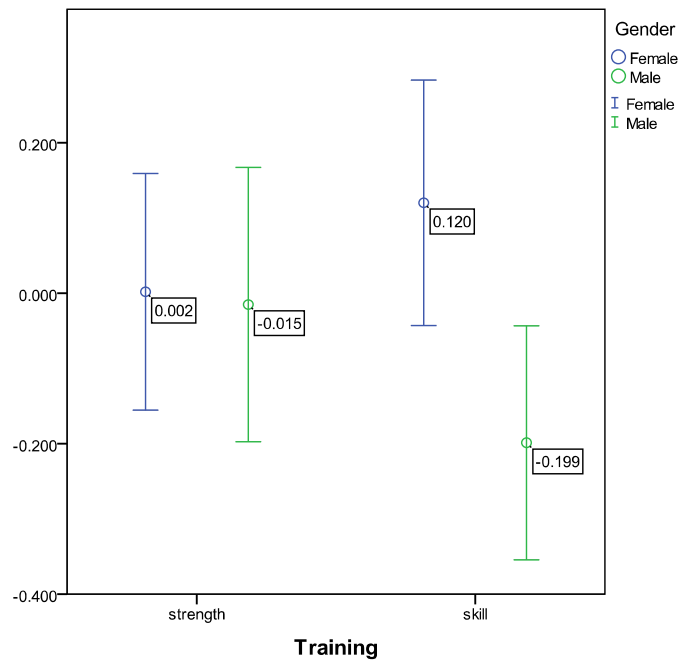


Figure 6.40 Sensor 3 (UES) duration (s): mean difference (post 2-week training minus baseline) and 95% CI around the mean, for each gender, by training group, in effortful 10 mL water swallowing task.

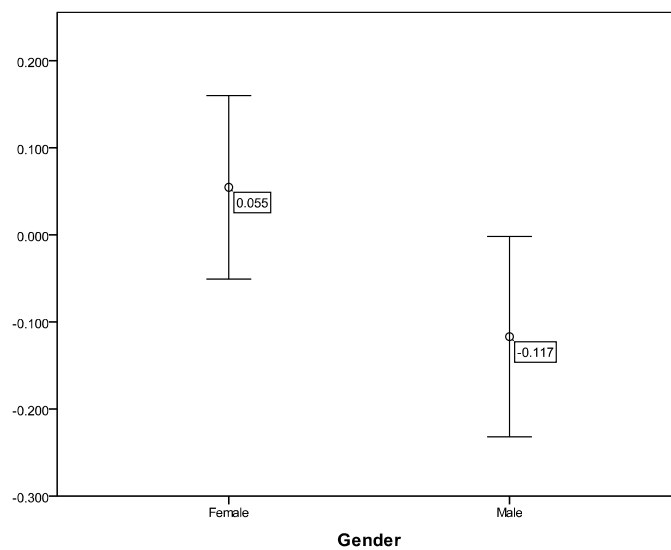


Figure 6.41 Sensor 3 (UES) duration (s): mean difference (post 2 weeks minus baseline) and 95% CI around the mean for each gender in effortful 10 mL water swallowing task.

Table 6.18 Sensor 3 (UES) duration (s) in effortful 10 mL water swallowing task: estimated mean difference (post training minus baseline), by TRAINING and GENDER

Training	Gender	Mean	95% Confidence Interval	
			Lower Bound	Upper Bound
STR	Female	0.002	-0.137	0.142
	Male	-0.015	-0.171	0.141
SKL	Female	0.147	-0.014	0.308
	Male	-0.197	-0.340	-0.055

Table 6.19 Sensor 3 (UES) duration (s) in effortful 10 mL water swallowing task: estimated mean difference (post training minus baseline), by GENDER

Gender	Mean	95% Confidence Interval	
		Lower Bound	Upper Bound
Female	0.075	-0.032	0.181
Male	-0.106	-0.212	-0.001

In SKL, the estimated mean difference was of 0.025 s (*SD* 0.259, *CI* [-0.133, 0.082]) decrease from baseline to post-training. In STR, the mean difference was of 0.006 s (*SD* 0.212, *CI* [-0.111, 0.098]) decrease from baseline to post-training. Effects sizes are reported in Table 6.20.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 3 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value minus baseline value) (SKL-I *n* = 10, 5 old and 5 young, 5 females and 5 males; SKL-D *n* = 8, 4 old and 4 young, 3 females and 5 males) (Table 6.22, p. 232). There was a significant effect of GENDER ($F(1, 14) = 10.34$, $p = 0.006$, Cohen's $d = 1.72$). This effect was already reported, under post hoc tests in SKL.

Sensor 3 (UES) duration in non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 3 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value minus baseline value) (SKL *n* = 18, 9 old and 9 young, 8 females and 10 males; STR *n* = 18, 9 old and 9 young, 10 females and 8 males). There were no significant effects (Table 6.21, p. 230).

In SKL, the estimated mean difference was of 0.066 s (*SD* 0.478, *CI* [-0.249, 0.117]) *decrease* from baseline to post-training. In STR, the mean difference was of 0.020 s (*SD* 0.188, *CI* [-0.159, 0.198]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.20.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 3 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I *n* = 10, 5 old and 5 young, 5 females and 5 males; SKL-D *n* = 8, 4 old and 4 young, 3 females and 5 males). There were no significant effects (Table 6.22, p. 232).

Sensor 3 (UES) duration in non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (duration of sensor 3 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL *n* = 17, 9 old and 8 young, 8 females and 9 males; STR *n* = 18, 9 old and 9 young, 10 females and 8 males). There were no significant effects (Table 6.21, p. 230).

In SKL, the estimated mean difference was of 0.002 s (*SD* 0.388, *CI* [-0.165, 0.161]) *decrease* from baseline to post-training. In STR, the mean difference was of 0.062 s (*SD* 0.238, *CI* [-0.214, 0.090]) *decrease* from baseline to post-training. Effects sizes are reported in Table 6.20.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (duration of sensor 3 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I *n* = 9, 5 old and 4 young, 5 females and 4 males; SKL-D *n* = 8, 4 old and 4 young, 3 females and 5 males). There were no significant effects (Table 6.22, p. 232).

Table 6.20 Effect size (Cohen's *d*) for the effect of training type (SKL *n* = 18, STR *n* = 18): sensor 3 (UES), pressure duration

Swallowing task	SKL	STR
Effortful saliva	0.25	0.17
Effortful 10 mL water	0.15	0.04
Non-effortful saliva	0.16	0.00
Non-effortful 10 mL water	0.07	0.23

Summary: Duration of the pressure events at sensor 3 (UES)

In the effortful saliva swallowing task, there was a significant interaction of TRAINING*GENDER. Males in SKL and Females in STR had a decrease in duration (both non-significant), but Males in STR and Females in SKL had little change in the duration of sensor 3 following training. There was also an interaction of TRAINING*AGE in the same task, where Old in STR and Young in SKL had a decrease in duration (both non-significant) but Young in STR and Old in SKL had little change.

In the effortful 10 mL water swallowing task, there was a significant effect of GENDER with Males demonstrating a decrease in duration, and Females an increase. The interaction of TRAINING*GENDER gives a further insight into the main effect of GENDER. In SKL there was a significant effect of GENDER with Males having a significant decrease in duration and Females a non-significant increase. In STR, both Females and Males had little change. Following STR and SKL, the effect sizes ranged from no effects to small effects.

**Table 6.21 Factor effects (F, df, p values GROUP (SKL vs. STR), GENDER, AGE (Young vs. Old):
Manometry absolute duration for sensor 1, 2 and 3 (significant results are in bold)**

Outcome measure	Swallowing task	Factors, F (df), p value
Sensor 1 - Duration	Effortful swallowing – saliva	TRAINING $F(1, 28) = 0.67, p = 0.42$ GENDER $F(1, 28) = 0.18, p = 0.67$ AGE $F(1, 28) = 0.05, p = 0.83$ TRAINING*GENDER $F(1, 28) = 0.54, p = 0.47$ TRAINING*AGE $F(1, 28) = 1.20, p = 0.28$ GENDER*AGE $F(1, 28) = 2.63, p = 0.11$ TRAINING*AGE*GENDER $F(1, 27) = 0.86, p = 0.36$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 28) = 3.57, p = 0.07$ GENDER $F(1, 28) = 0.36, p = 0.55$ AGE $F(1, 28) = 0.85, p = 0.36$ TRAINING*GENDER $F(1, 28) = 0.03, p = 0.85$ TRAINING*AGE $F(1, 28) = 1.41, p = 0.24$ GENDER*AGE $F(1, 28) = 0.32, p = 0.57$ TRAINING*AGE*GENDER $F(1, 28) = 0.01, p = 0.91$
	Non-effortful swallowing – saliva	TRAINING $F(1, 28) = 0.73, p = 0.40$ GENDER $F(1, 28) = 0.07, p = 0.78$ AGE $F(1, 28) = 0.02, p = 0.88$

		<p>TRAINING*GENDER $F(1, 28) = 1.46, p = 0.23$</p> <p>TRAINING*AGE $F(1, 28) = 4.11, p = 0.052$</p> <p>GENDER*AGE $F(1, 28) = 1.23, p = 0.27$</p> <p>TRAINING*AGE*GENDER $F(1, 28) = 0.14, p = 0.71$</p>
	Non-effortful swallowing – 10 mL water	<p>TRAINING $F(1, 28) = 0.27, p = 0.60$</p> <p>GENDER $F(1, 28) = 0.09, p = 0.76$</p> <p>AGE $F(1, 28) = 0.53, p = 0.47$</p> <p>TRAINING*GENDER $F(1, 28) = 2.14, p = 0.15$</p> <p>TRAINING*AGE $F(1, 28) = 0.09, p = 0.76$</p> <p>GENDER*AGE $F(1, 28) = 0.00, p = 0.95$</p> <p>TRAINING*AGE*GENDER $F(1, 28) = 0.31, p = 0.58$</p>
Sensor 2 - Duration	Effortful swallowing – saliva	<p>TRAINING $F(1, 28) = 0.12, p = 0.73$</p> <p>GENDER $F(1, 28) = 0.11, p = 0.74$</p> <p>AGE $F(1, 28) = 0.06, p = 0.81$</p> <p>TRAINING*GENDER $F(1, 28) = 3.22, p = 0.08$</p> <p>TRAINING*AGE $F(1, 28) = 0.15, p = 0.69$</p> <p>GENDER*AGE $F(1, 28) = 0.32, p = 0.57$</p> <p>TRAINING*AGE*GENDER $F(1, 27) = 1.57, p = 0.22$</p>
	Effortful swallowing – 10 mL water	<p>TRAINING $F(1, 28) = 1.50, p = 0.23$</p> <p>GENDER $F(1, 28) = 0.26, p = 0.61$</p> <p>AGE $F(1, 28) = 3.56, p = 0.07$</p> <p>TRAINING*GENDER $F(1, 28) = 0.06, p = 0.81$</p> <p>TRAINING*AGE $F(1, 28) = 0.46, p = 0.50$</p> <p>GENDER*AGE $F(1, 28) = 0.40, p = 0.53$</p> <p>TRAINING*AGE*GENDER $F(1, 28) = 0.38, p = 0.54$</p>
	Non-effortful swallowing – saliva	<p>TRAINING $F(1, 28) = 0.92, p = 0.34$</p> <p>GENDER $F(1, 28) = 0.68, p = 0.42$</p> <p>AGE $F(1, 28) = 0.52, p = 0.47$</p> <p>TRAINING*GENDER $F(1, 28) = 0.06, p = 0.80$</p> <p>TRAINING*AGE $F(1, 28) = 0.40, p = 0.53$</p> <p>GENDER*AGE $F(1, 28) = 1.10, p = 0.30$</p> <p>TRAINING*AGE*GENDER $F(1, 27) = 0.003, p = 0.96$</p>
	Non-effortful swallowing – 10 mL water	<p>TRAINING $F(1, 28) = 0.00, p = 1.00$</p> <p>GENDER $F(1, 28) = 0.62, p = 0.43$</p> <p>AGE $F(1, 28) = 2.34, p = 0.14$</p> <p>TRAINING*GENDER $F(1, 28) = 1.46, p = 0.23$</p> <p>TRAINING*AGE $F(1, 28) = 3.05, p = 0.09$</p> <p>GENDER*AGE $F(1, 28) = 1.84, p = 0.18$</p> <p>TRAINING*AGE*GENDER $F(1, 28) = 0.35, p = 0.55$</p>

Sensor 3 - Duration	Effortful swallowing – saliva	<p>TRAINING $F(1, 27) = 1.06, p = 0.31$</p> <p>GENDER $F(1, 27) = 0.07, p = 0.78$</p> <p>AGE $F(1, 27) = 0.44, p = 0.51$</p> <p>TRAINING*GENDER $F(1, 27) = 4.71, p = 0.039$</p> <p>TRAINING*AGE $F(1, 27) = 4.33, p = 0.047$</p> <p>GENDER*AGE $F(1, 27) = 1.30, p = 0.26$</p> <p>TRAINING*AGE*GENDER $F(1, 27) = 0.19, p = 0.66$</p>
	Effortful swallowing – 10 mL water	<p>TRAINING $F(1, 28) = 0.06, p = 0.80$</p> <p>GENDER $F(1, 28) = 6.09, p = 0.02$</p> <p>AGE $F(1, 28) = 1.91, p = 0.18$</p> <p>GENDER*TRAINING $F(1, 28) = 4.99, p = 0.034$</p> <p>TRAINING*AGE $F(1, 28) = 0.00, p = 0.98$</p> <p>GENDER*AGE $F(1, 28) = 0.03, p = 0.87$</p> <p>TRAINING*AGE*GENDER $F(1, 28) = 1.94, p = 0.17$</p>
	Non-effortful swallowing – saliva	<p>TRAINING $F(1, 28) = 0.47, p = 0.49$</p> <p>GENDER $F(1, 28) = 0.33, p = 0.57$</p> <p>AGE $F(1, 28) = 0.04, p = 0.84$</p> <p>TRAINING*GENDER $F(1, 28) = 1.79, p = 0.19$</p> <p>TRAINING*AGE $F(1, 28) = 0.28, p = 0.60$</p> <p>GENDER*AGE $F(1, 28) = 2.10, p = 0.16$</p> <p>TRAINING*AGE*GENDER $F(1, 28) = 0.64, p = 0.43$</p>
	Non-effortful swallowing – 10 mL water	<p>TRAINING $F(1, 27) = 0.30, p = 0.58$</p> <p>GENDER $F(1, 27) = 2.12, p = 0.15$</p> <p>AGE $F(1, 27) = 2.80, p = 0.11$</p> <p>TRAINING*GENDER $F(1, 27) = 2.52, p = 0.12$</p> <p>TRAINING*AGE $F(1, 27) = 0.01, p = 0.92$</p> <p>GENDER*AGE $F(1, 27) = 1.29, p = 0.26$</p> <p>TRAINING*AGE*GENDER $F(1, 27) = 0.37, p = 0.54$</p>

Table 6.22 Factors effects (F , df , p values): GROUP (SKL-I vs. SKL-D), GENDER, AGE (Young vs. Old): Manometry absolute duration for sensor 1, 2 and 3 (significant results are in bold)

Outcome measure	Swallowing task	Swallowing task
Sensor 1 – Duration	Effortful swallowing – saliva	<p>TRAINING $F(1, 14) = 0.07, p = 0.79$</p> <p>GENDER $F(1, 14) = 0.08, p = 0.77$</p> <p>AGE $F(1, 14) = 1.38, p = 0.26$</p>
	Effortful	TRAINING $F(1, 14) = 0.77, p = 0.39$

	swallowing – 10 mL water	GENDER $F(1, 14) = 1.21, p = 0.29$ AGE $F(1, 14) = 0.07, p = 0.78$
	Non-effortful swallowing – saliva	TRAINING $F(1, 14) = 0.81, p = 0.38$ GENDER $F(1, 14) = 0.46, p = 0.51$ AGE $F(1, 14) = 0.90, p = 0.36$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 0.54, p = 0.47$ GENDER $F(1, 14) = 0.87, p = 0.36$ AGE $F(1, 14) = 0.31, p = 0.58$
Sensor 2 – Duration	Effortful swallowing – saliva	TRAINING $F(1, 14) = 1.56, p = 0.23$ GENDER $F(1, 14) = 1.71, p = 0.21$ AGE $F(1, 14) = 0.13, p = 0.72$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 4.24, p = 0.06$ GENDER $F(1, 14) = 0.01, p = 0.93$ AGE $F(1, 14) = 2.26, p = 0.15$
	Non-effortful swallowing – saliva	TRAINING $F(1, 14) = 0.35, p = 0.56$ GENDER $F(1, 14) = 1.45, p = 0.25$ AGE $F(1, 14) = 2.75, p = 0.12$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 0.12, p = 0.74$ GENDER $F(1, 14) = 3.21, p = 0.09$ AGE $F(1, 14) = 9.41, p = 0.01$
Sensor 3 – Duration	Effortful swallowing – saliva	TRAINING $F(1, 13) = 2.12, p = 0.17$ GENDER $F(1, 13) = 1.67, p = 0.22$ AGE $F(1, 13) = 2.81, p = 0.12$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 2.03, p = 0.17$ GENDER $F(1, 14) = 10.34, p = 0.006$ AGE $F(1, 14) = 0.70, p = 0.42$
	Non-effortful swallowing – saliva	TRAINING $F(1, 14) = 0.12, p = 0.74$ GENDER $F(1, 14) = 0.96, p = 0.34$ AGE $F(1, 14) = 0.00, p = 0.97$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 13) = 1.63, p = 0.22$ GENDER $F(1, 13) = 2.06, p = 0.17$ AGE $F(1, 13) = 0.64, p = 0.44$

6.2.1.4 *Relative timing measurements*

6.2.1.4.1 *Relative duration between peak amplitude of sensor 1 (upper pharynx) to peak amplitude of sensor 2 (mid-pharynx)*

Relative duration between peak of sensor 1 (upper pharynx) to the peak of sensor 2 (mid-pharynx) in effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (timing between peak sensor 1 to peak sensor 2 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.27, p. 243).

In SKL, the estimated mean difference was of 0.028 s (*SD* 0.107, *CI* [-0.086, 0.031]) *decrease* from baseline to post-training. In STR, the mean difference was of 0.039 s (*SD* 0.121, *CI* [-0.096, 0.017]) *decrease* from baseline to post-training. Effects sizes are reported in Table 6.23.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (timing between peak sensor 1 to peak sensor 2 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.28, p. 245).

Relative duration between peak of sensor 1 (upper pharynx) to the peak of sensor 2 (mid-pharynx) in effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (timing between peak sensor 1 to peak sensor 2 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.27, p. 243).

In SKL, the estimated mean difference was of 0.004 s (*SD* 0.065, *CI* [-0.049, 0.058]) *increase* from baseline to post-training. In STR, the mean difference was of 0.030 s (*SD* 0.132, *CI* [-0.082, 0.022]) *decrease* from baseline to post-training. Effects sizes are reported in Table 6.23.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (timing between peak sensor 1 to peak sensor 2 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.28,

p. 245). There was a marginally significant effect of GENDER ($F(1, 14) = 3.78, p = 0.07$, Cohen's $d = 1.00$), with Females having an increase in duration and Males having a decrease in relative duration following training (Figure 6.42).

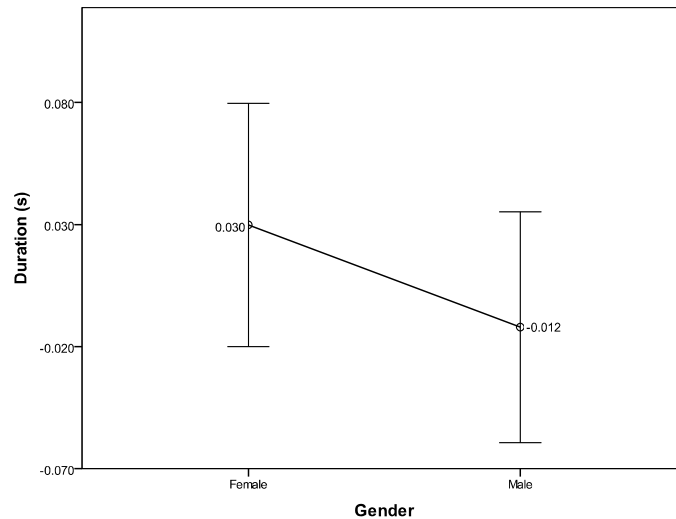


Figure 6.42 Time duration between peak of sensor 1 (upper pharynx) to the peak of sensor 2 (mid-pharynx) in effortful 10 mL water swallowing task: mean difference (post training minus baseline), and 95% CI, by gender.

Relative duration between peak of sensor 1 (upper pharynx) to the peak of sensor 2 (mid-pharynx) in non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (timing between peak sensor 1 to peak sensor 2 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.27, p. 243).

There was a significant effect of GENDER*AGE ($F(1, 28) = 4.62, p = 0.04$, Cohen's $d = 0.81$). In Young, Females and Males had similar mean difference (Cohen's d for the effect of Gender in Young = 0.25). In Old, Females had an increase in the time duration, whereas Males had little change (Cohen's d for the effect of Gender in Old = 1.17). In order to test if the difference in relative duration in older females was significant, a paired-samples t-test was conducted. There was a significant change in relative duration in non-effortful saliva swallowing with 0.083 s increase ($CI [0.030, 0.135], t(7) = 3.73, p = 0.007$).

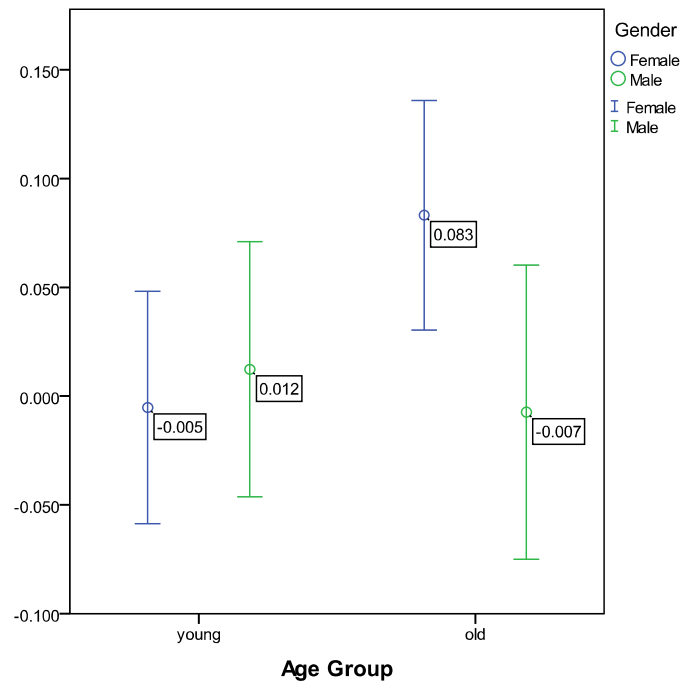


Figure 6.43 Time duration (s) between peak of sensor 1 (upper pharynx) to peak of sensor 2 (mid-pharynx) in non-effortful saliva swallowing: mean difference of change following training, 95% CI around the mean.

In SKL, the estimated mean difference was of 0.041 s (*SD* 0.089, *CI* [0.002, 0.081]) increase from baseline to post-training. In STR, the mean difference was of 0.003 s (*SD* 0.075, *CI* [-0.036, 0.042]) increase from baseline to post-training. Effects sizes are reported in Table 6.23.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (timing between peak sensor 1 to peak sensor 2 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.28, p. 245).

Relative duration between peak of sensor 1 (upper pharynx) to the peak of sensor 2 (mid-pharynx) in non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (timing between peak sensor 1 to peak sensor 2 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.27, p. 243).

In SKL, the estimated mean difference was of 0.012 s (*SD* 0.058, *CI* [-0.016, 0.040]) *increase* from baseline to post-training. In STR, the mean difference was of 0.008 s (*SD* 0.052, *CI* [-0.036, 0.019]) *decrease* from baseline to post-training. Effects sizes are reported in Table 6.23.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (timing between peak sensor 1 to peak sensor 2 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.28, p. 245).

Table 6.23 Effect size (Cohen's *d*) for the effect of training type (SKL *n* = 18, STR *n* = 18): time duration between peak of sensor 1 (upper pharynx) to the peak of sensor 2 (mid-pharynx)

Swallowing task	SKL	STR
Effortful saliva	0.29	0.33
Effortful 10 mL water	0.00	0.18
Non-effortful saliva	0.41	0.00
Non-effortful 10 mL water	0.17	0.13

Summary: Relative time duration between peak amplitude of sensor 1 (upper pharynx) to peak amplitude of sensor 2 (mid-pharynx)

To summarize, there was no significant differences between SKL to STR, and between SKL subgroups in relative time duration between peak amplitude of sensor 1 (upper pharynx) to peak amplitude of sensor 2 (mid-pharynx). In the effortful 10 mL water swallowing task, there was a marginally significant effect of GENDER with Females having an increase in duration and Males having a decrease following training. In non-effortful saliva there was a significant effect of GENDER*AGE. Older females had significantly longer relative time duration between peak amplitude of sensor 1 (upper pharynx) to peak amplitude of sensor 2 (mid-pharynx).

6.2.1.4.2 Relative duration between onset of pressure change in sensor 1 (upper pharynx) and the onset of pressure change in sensor 3 (UES)

Time duration between onset of pressure activity of sensor 1 (upper pharynx) to the onset of pressure activity of sensor 3 (UES) in effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (timing between onset of sensor 1 to onset of sensor 3 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL $n = 17$, 9 old and 8 young, 8 females and 9 males; STR $n = 18$, 9 old and 9 young, 10 females and 8 males) (Table 6.27, p. 243).

There were significant effects of TRAINING*AGE ($F(1, 27) = 4.32, p = 0.047$, Cohen's $d = 0.62$) (Table 6.24), and TRAINING*GENDER ($F(1, 27) = 6.70, p = 0.015$, Cohen's $d = 0.99$) (Table 6.25). The interaction of TRAINING*AGE is presented in Figure 6.44. Old in STR training and Young in SKL training had an increase in duration, while Young in STR training and Old in SKL had little change in the time duration between the onset of sensor 1 to onset of sensor 3. To explore the changes in Old subjects following STR and in Young following SKL, a paired t-test was conducted. For Young in SKL there was no significant change ($t(7) = 1.24, p = 0.25$), and for Old in STR there was no significant change as well ($t(8) = 1.60, p = 0.15$).

The interaction of TRAINING*GENDER is presented in Figure 6.45. Males in SKL training had an increase in duration, but Females – little change (Cohen's d for the effect of GENDER in SKL = 0.57). Following STR training, Females had an increase but Males had little change in the time duration between the onset of sensor 1 to onset of sensor 3 (Cohen's d for the effect of GENDER in STR = 1.20). To further explore the changes in Females in STR training and Males in SKL training paired-samples t-tests were conducted. For Females following STR, there was a significant increase in relative duration of 0.164 s ($CI [0.000, 0.329], t(9) = 2.27, p = 0.049$). For Males on SKL, there was no significant change in the relative time duration ($t(8) = 1.40, p = 0.20$).

Table 6.24 Estimated means for the time duration (s) between onset of pressure activity of sensor 1 (upper pharynx) to the onset of pressure activity of sensor 3 (UES) in effortful saliva swallowing task, by training and age group

Training	Age group	Mean	95% Confidence Interval	
			Lower Bound	Upper Bound
STR	Young	-0.030	-0.222	0.161
	Old	0.125	-0.067	0.317
SKL	Young	0.256	0.047	0.465
	Old	0.008	-0.194	0.211

Table 6.25 Estimated means for the time duration (s) between onset of pressure activity of sensor 1 (upper pharynx) to the onset of pressure activity of sensor 3 (UES) in effortful saliva swallowing task, by training and gender

Training	Gender	Mean	95% Confidence Interval	
			Lower Bound	Upper Bound
STR	Female	0.165	-0.016	0.346
	Male	-0.070	-0.273	0.132
SKL	Female	-0.001	-0.210	0.208
	Male	0.265	0.063	0.467

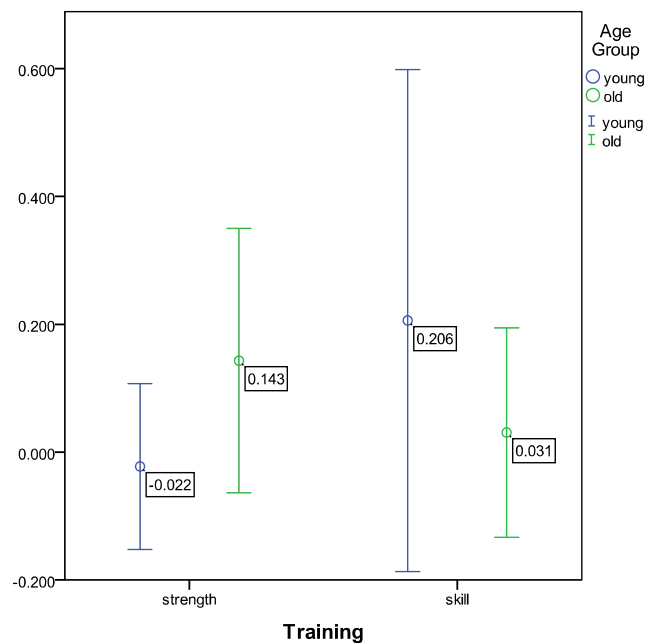


Figure 6.44 Time duration (s) between onset of pressure activity of sensor 1 (upper pharynx) to the onset of pressure activity of sensor 3 (UES) in effortful saliva swallowing task: mean difference in duration (post training minus baseline) and 95% CI around the mean, for each age group, by training type.

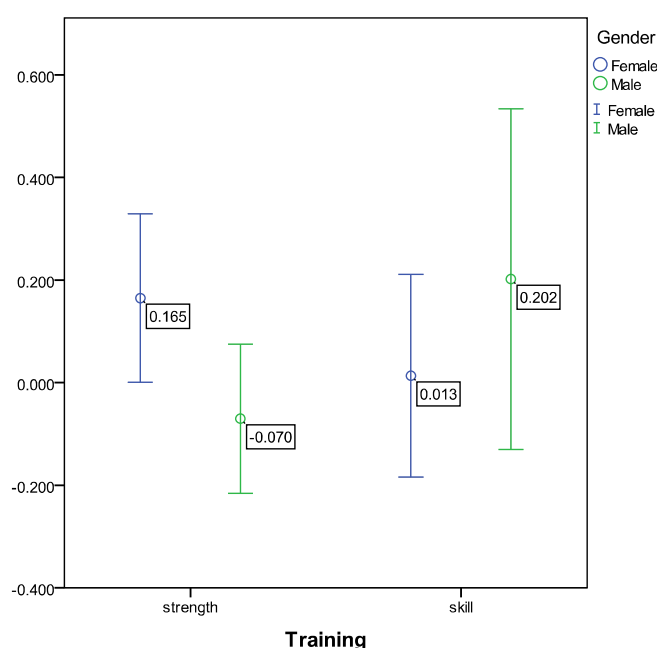


Figure 6.45 Time duration (s) between onset of pressure activity of sensor 1 (upper pharynx) to the onset of pressure activity of sensor 3 (UES) in effortful saliva swallowing task: mean difference in duration (post training minus baseline) and 95% CI around the mean, for each gender, by training type.

In SKL, the estimated mean difference was of 0.132 s (SD 0.356, CI [-0.013, 0.277]) increase from baseline to post-training. In STR, the mean difference was of 0.047 s (SD 0.234, CI [-0.088, 0.183]) increase from baseline to post-training. Effects sizes are reported in Table 6.26.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (timing between onset of sensor 1 to onset of sensor 3 in effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I $n = 10$, 5 old and 5 young, 5 females and 5 males; SKL-D $n = 7$, 4 old and 3 young, 3 females and 4 males). There were no significant effects (Table 6.28, p. 245).

Time between onset of pressure change in sensor 1 (upper pharynx) to the onset of pressure change in sensor 3 (UES) for effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (timing between onset of sensor 1 to onset of sensor 3 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL $n = 18$, 9 old and 9 young, 8 females and 10 males; STR $n = 18$, 9 old and 9 young, 10 females and 8 males). There were no significant effects (Table 6.27, p. 243).

In SKL, the estimated mean difference was of 0.105 s (SD 0.287, CI [-0.016, 0.226]) *increase* from baseline to post-training. In STR, the mean difference was of 0.049 s (SD 0.178, CI [-0.069, 0.167]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.26.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (timing between onset of sensor 1 to onset of sensor 3 in effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I $n = 10$, 5 old and 5 young, 5 females and 5 males; SKL-D $n = 8$, 4 old and 4 young, 3 females and 5 males). There were no significant effects (Table 6.28, p. 245).

Time between onset of pressure change in sensor 1 (upper pharynx) to the onset of pressure change in sensor 3 (UES) for non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (timing between onset of sensor 1 to onset of sensor 3 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL $n = 18$, 9 old and 9 young, 8 females and 10 males; STR $n = 18$, 9 old and 9 young, 10 females and 8 males). There were no significant effects (Table 6.27, p. 243).

In SKL, the estimated mean difference was of 0.039 s (SD 0.306, CI [-0.075, 0.153]) *increase* from baseline to post-training. In STR, the mean difference was of 0.046 s (SD 0.091, CI [-0.065, 0.157]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.26.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (timing between onset of sensor 1 to onset of sensor 3 in non-effortful saliva swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I $n = 10$, 5 old and 5 young, 5 females and 5 males; SKL-D $n = 8$, 4 old and 4 young, 3 females and 5 males). There were no significant effects (Table 6.28, p. 245).

Time duration between onset of pressure activity of sensor 1 (upper pharynx) to the onset of pressure activity of sensor 3 (UES) in non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (timing between onset of sensor 1 to onset of sensor 3 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). (SKL $n = 17$, 9 old and 8 young, 8

females and 9 males; STR n = 18, 9 old and 9 young, 10 females and 8 males). There were no significant effects (Table 6.27, p. 243).

In SKL, the estimated mean difference was of 0.021 s (*SD* 0.207, *CI* [-0.061, 0.104]) *increase* from baseline to post-training. In STR, the mean difference was of 0.035 s (*SD* 0.104, *CI* [-0.042, 0.112]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.26.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (timing between onset of sensor 1 to onset of sensor 3 in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I n = 9, 5 old and 4 young, 5 females and 4 males; SKL-D n = 8, 4 old and 4 young, 3 females and 5 males). There were no significant effects (Table 6.28, p. 245).

Table 6.26 Effect size (Cohen's *d*) for the effect of training type (SKL n = 18, STR n = 18): time duration between onset of pressure activity of sensor 1 (upper pharynx) to the onset of pressure activity of sensor 3 (UES)

Swallowing task	SKL	STR
Effortful saliva	0.26	0.30
Effortful 10 mL water	0.44	0.30
Non-effortful saliva	0.24	0.35
Non-effortful 10 mL water	0.05	0.24

Summary: Time duration between onset of sensor 1 (upper pharynx) pressure activity to the onset of sensor 3 (UES) pressure activity

In effortful saliva swallowing, Old in STR and Young in SKL had a increase in relative duration, but Young in STR and Old in SKL had little change. Additional analyses revealed that the changes for Old in STR and for Young in SKL were no significant.

In addition, Females in STR and Males in SKL had an increase in relative duration following training, while Males in STR and Females in SKL had little change in the time duration between the onset of sensor 1 to onset of sensor 3. Additional analyses revealed that the changes for Females following STR, there was a significant increase in relative duration, but for Males in SKL, there was no significant change. There were small effect sizes of training for STR. For SKL there were zero to small-medium effect sizes.

**Table 6.27 Factor effects (*F*, *df*, *p* values): *GROUP* (SKL vs. STR), *GENDER*, *AGE* (Young vs. Old):
Timing measurements (relative duration, in s) of the pharyngeal pressure events (significant results are
in bold)**

Outcome measure	Task	Factors, <i>F</i> (df), <i>p</i> value
Peak amplitude of sensor 1 - peak amplitude of sensor 2 – Duration	Effortful swallowing – saliva	TRAINING $F(1, 28) = 0.09, p = 0.77$ GENDER $F(1, 28) = 0.85, p = 0.36$ AGE $F(1, 28) = 0.57, p = 0.45$ TRAINING*GENDER $F(1, 28) = 0.06, p = 0.80$ TRAINING*AGE $F(1, 28) = 1.47, p = 0.23$ GENDER*AGE $F(1, 28) = 1.42, p = 0.24$ TRAINING*AGE*GENDER $F(1, 28) = 0.69, p = 0.41$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 28) = 0.88, p = 0.35$ GENDER $F(1, 28) = 2.02, p = 0.16$ AGE $F(1, 28) = 0.53, p = 0.47$ TRAINING*GENDER $F(1, 28) = 0.01, p = 0.94$ TRAINING*AGE $F(1, 28) = 0.09, p = 0.76$ GENDER*AGE $F(1, 28) = 0.00, p = 0.99$ TRAINING*AGE*GENDER $F(1, 28) = 1.64, p = 0.21$
	Non-effortful swallowing – saliva	TRAINING $F(1, 28) = 2.01, p = 0.17$ GENDER $F(1, 28) = 2.26, p = 0.14$ AGE $F(1, 28) = 1.89, p = 0.18$ TRAINING*GENDER $F(1, 28) = 0.15, p = 0.70$ TRAINING*AGE $F(1, 28) = 0.01, p = 0.92$ GENDER*AGE $F(1, 28) = 4.62, p = 0.04$ TRAINING*AGE*GENDER $F(1, 28) = 0.20, p = 0.66$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 28) = 1.13, p = 0.30$ GENDER $F(1, 28) = 2.47, p = 0.13$ AGE $F(1, 28) = 0.50, p = 0.48$ TRAINING*GENDER $F(1, 28) = 0.37, p = 0.55$ TRAINING*AGE $F(1, 28) = 1.37, p = 0.25$ GENDER*AGE $F(1, 28) = 0.76, p = 0.39$ TRAINING*AGE*GENDER $F(1, 28) = 0.11, p = 0.74$
Onset of sensor 1 - sensor 3 - Duration	Effortful swallowing – saliva	TRAINING $F(1, 27) = 0.77, p = 0.39$ GENDER $F(1, 27) = 0.03, p = 0.87$ AGE $F(1, 27) = 0.22, p = 0.64$ TRAINING*GENDER $F(1, 27) = 6.70, p = 0.015$ TRAINING*AGE $F(1, 27) = 4.32, p = 0.047$ GENDER*AGE $F(1, 27) = 1.34, p = 0.26$

		TRAINING*AGE*GENDER $F(1, 28) = 0.04, p = 0.84$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 28) = 0.46, p = 0.50$ GENDER $F(1, 28) = 1.18, p = 0.28$ AGE $F(1, 28) = 0.00, p = 0.98$ TRAINING*GENDER $F(1, 28) = 1.67, p = 0.21$ TRAINING*AGE $F(1, 28) = 1.27, p = 0.27$ GENDER*AGE $F(1, 28) = 0.01, p = 0.91$ TRAINING*AGE*GENDER $F(1, 28) = 0.18, p = 0.67$
	Non-effortful swallowing – saliva	TRAINING $F(1, 28) = 0.01, p = 0.92$ GENDER $F(1, 28) = 1.42, p = 0.24$ AGE $F(1, 28) = 0.02, p = 0.89$ TRAINING*GENDER $F(1, 28) = 3.40, p = 0.076$ TRAINING*AGE $F(1, 28) = 0.02, p = 0.88$ GENDER*AGE $F(1, 28) = 0.01, p = 0.94$ TRAINING*AGE*GENDER $F(1, 28) = 0.06, p = 0.81$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 27) = 0.06, p = 0.81$ GENDER $F(1, 27) = 2.19, p = 0.15$ AGE $F(1, 27) = 1.73, p = 0.20$ TRAINING*GENDER $F(1, 27) = 2.37, p = 0.13$ TRAINING*AGE $F(1, 27) = 0.00, p = 0.98$ GENDER*AGE $F(1, 27) = 2.05, p = 0.16$ TRAINING*AGE*GENDER $F(1, 27) = 1.10, p = 0.30$

Table 6.28 Factor effects (*F*, *df*, *p* values): GROUP (SKL-I vs. SKL-D), GENDER, AGE (Young vs. Old): Timing measurements (relative duration, in s) of the pharyngeal pressure events (significant results are in bold)

Outcome measure	Task	Factors, <i>F</i> (<i>df</i>), <i>p</i> value
Peak amplitude of sensor 1 - peak amplitude of sensor 2 – Duration	Effortful swallowing – saliva	TRAINING $F(1, 14) = 0.13, p = 0.72$ GENDER $F(1, 14) = 0.27, p = 0.61$ AGE $F(1, 14) = 2.09, p = 0.17$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 1.83, p = 0.20$ GENDER $F(1, 14) = 3.78, p = 0.07$ AGE $F(1, 14) = 2.42, p = 0.14$
	Non-effortful swallowing – saliva	TRAINING $F(1, 14) = 0.51, p = 0.48$ GENDER $F(1, 14) = 1.29, p = 0.27$ AGE $F(1, 14) = 0.36, p = 0.56$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 1.34, p = 0.26$ GENDER $F(1, 14) = 0.62, p = 0.44$ AGE $F(1, 14) = 0.05, p = 0.82$
Onset of sensor 1 - sensor 3 – Duration	Effortful swallowing – saliva	TRAINING $F(1, 13) = 1.23, p = 0.28$ GENDER $F(1, 13) = 2.12, p = 0.17$ AGE $F(1, 13) = 2.29, p = 0.15$
	Effortful swallowing – 10 mL water	TRAINING $F(1, 14) = 1.94, p = 0.18$ GENDER $F(1, 14) = 1.67, p = 0.21$ AGE $F(1, 14) = 0.66, p = 0.43$
	Non-effortful swallowing – saliva	TRAINING $F(1, 14) = 0.75, p = 0.40$ GENDER $F(1, 14) = 2.23, p = 0.16$ AGE $F(1, 14) = 0.03, p = 0.87$
	Non-effortful swallowing – 10 mL water	TRAINING $F(1, 13) = 2.63, p = 0.13$ GENDER $F(1, 13) = 1.61, p = 0.22$ AGE $F(1, 13) = 0.33, p = 0.57$

6.2.1.5 Four-week training

Data were collected for 9/10 subjects. One subjects had missing data due to intolerance to catheter placement (intolerance was present at baseline and at post 2-week training as well). In addition, manometry pressure from sensor 3 (UES) for two tasks: effortful saliva and non-effortful water swallowing was available for all of the above except one. Missing data for the additional one participant was due to nadir pressures that were defined as outliers (greater than 3 *SD* from the sample mean) and were removed from the analysis.

Due to low number of participants, SKL subgroups were analyzed together as one group ($n = 6$), using Friedman's ANOVAs (non-parametric) for related means (pre-training, post 2-week training and post 4-week training). STR group were not analyzed since it consisted on three participants only. Raw data for this group is presented in Appendix 7.

6.2.1.5.1 *Peak amplitude pressure*

The raw data for peak pressure in all three sensors (1-3) during all four tasks: effortful saliva, effortful water swallowing, non-effortful saliva, and non-effortful water swallowing are presented in Appendix 7. None of the results was statistically significant (Table 6.29).

Table 6.29 Friedman's ANOVA results: Pressure measurements – 4-week protocol, in SKL ($n = 6$)
(significant results are in bold)

<i>Measure</i>	<i>Task</i>	<i>Friedman's ANOVA result</i>
Peak amplitude of the pressure event at sensor 1 (upper pharynx)	Effortful saliva swallowing	$\chi^2(2) = 2.33, p = 0.43$
	Effortful 10 mL water swallowing	$\chi^2(2) = 4.00, p = 0.18$
	Non-effortful saliva swallowing	$\chi^2(2) = 1.33, p = 0.57$
	Non-effortful 10 mL water swallowing	$\chi^2(2) = 5.33, p = 0.72$
Peak amplitude of the pressure event at sensor 2 (mid-pharynx)	Effortful saliva swallowing	$\chi^2(2) = 0.33, p = 0.95$
	Effortful 10 mL water swallowing	$\chi^2(2) = 1.33, p = 0.57$
	Non-effortful saliva swallowing	$\chi^2(2) = 0.00, p = 1.00$
	Non-effortful 10 mL water swallowing	$\chi^2(2) = 1.33, p = 0.57$
Nadir pressure at sensor 3 (UES)	Effortful saliva swallowing	$\chi^2(2) = 1.33, p = 0.57$
	Effortful 10 mL water swallowing	$\chi^2(2) = 4.00, p = 0.18$
	Non-effortful saliva swallowing	$\chi^2(2) = 1.00, p = 0.74$
	Non-effortful 10 mL water swallowing	$\chi^2(2) = 2.80, p = 0.37$

6.2.1.5.2 Pressure events durations

The raw data for pressure duration of all three sensors (1-3) during all four tasks: effortful saliva, effortful water swallowing, non-effortful saliva, and non-effortful water swallowing are presented in Appendix 7. The results of the statistical analysis are presented in Table 6.30. Significant results are reported below.

Duration of the pressure event at sensor 2 (mid-pharynx)

In the effortful 10 mL water swallowing task, there was a significant difference between the three time points ($\chi^2(2) = 7.00$, $p = 0.029$, baseline: mean 0.397, SD 0.144; post 2 weeks: mean 0.542, SD 0.158; post 4 weeks: mean 0.482, SD 0.153, in SKL $n = 6$). Post hoc analysis was conducted in SKL using the Wilcoxon signed-rank test for related means (non-parametric). There was no significant differences between baseline to post 4 weeks ($z = -0.94$, $p = 0.44$) and there was no significant differences between post 2 weeks to post 4 weeks ($z = -0.73$, $p = 0.56$).

In the non-effortful 10 mL water swallowing task, there was a significant difference between the 3 time points ($\chi^2(2) = 7.91$, $p = 0.017$, baseline: mean 0.271, SD 0.085; post 2 weeks: mean 0.402, SD 0.128; post 4 weeks: mean 0.444, SD 0.286, in SKL $n = 6$). Post hoc analysis was conducted in SKL using the non-parametric Wilcoxon signed-rank test for related means. There was a marginally significant difference between baseline to post 4 weeks ($z = -2.03$, $p = 0.063$) and there was no significant difference between post 2 weeks to post 4 weeks ($z = -0.11$, $p = 1.00$).

There was a marginally significant trend towards increase in duration of sensor 3 (UES) activity during non-effortful saliva swallowing task ($p = 0.07$, baseline: mean 0.952, SD 0.104; post 2-week training: mean 1.180, SD 0.367; post 4 weeks: mean 1.251, SD 0.389), and during non-effortful 10 mL water swallowing ($p = 0.09$, baseline: mean 1.046, SD 0.087; post 2 weeks: mean 1.342, SD 0.347; post 4 weeks: mean 1.443, SD 0.214).

Table 6.30 Friedman's ANOVA results: Pressure duration – 4-week protocol, in SKL ($n = 6$) (significant results are in bold)

Measure	Task	Friedman's ANOVA Result
Duration of the pressure event at sensor 1 (upper pharynx)	Effortful saliva swallowing	$\chi^2(2) = 1.33$, $p = 0.57$
	Effortful 10 mL water swallowing	$\chi^2(2) = 1.00$, $p = 0.74$
	Non-effortful saliva swallowing	$\chi^2(2) = 3.21$, $p = 0.24$

	Non-effortful 10 mL water swallowing	$\chi^2(2) = 1.00, p = 0.74$
Duration of the pressure event at sensor 2 (mid-pharynx)	Effortful saliva swallowing	$\chi^2(2) = 1.33, p = 0.57$
	Effortful 10 mL water swallowing	$\chi^2(2) = 7.00, p = 0.029$
	Non-effortful saliva swallowing	$\chi^2(2) = 2.33, p = 0.43$
	Non-effortful 10 mL water swallowing	$\chi^2(2) = 7.91, p = 0.017$
Duration of the pressure event at sensor 3 (UES)	Effortful saliva swallowing	$\chi^2(2) = 1.33, p = 0.57$
	Effortful 10 mL water swallowing	$\chi^2(2) = 4.00, p = 0.18$
	Non-effortful saliva swallowing	$\chi^2(2) = 5.33, p = 0.07$
	Non-effortful 10 mL water swallowing	$\chi^2(2) = 5.20, p = 0.09$

6.2.1.5.3 *Relative duration measurements*

The raw data for relative durations (pharyngeal pressure timing measurements) during effortful saliva effortful water swallowing, non-effortful saliva, and non-effortful water swallowing are presented in Appendix 7. Table 6.31 presents the results of Friedman's ANOVA in SKL ($n = 6$). There was no significant effect of training.

Table 6.31 Friedman's ANOVA results: Timing of pressure– 4-week protocol, in SKL ($n = 6$) (significant results are in bold)

Measure	Task	Friedman's ANOVA result
Time duration between peak pressure of the upper pharynx (sensor 1) and peak amplitude of the mid-pharynx (sensor 2)	Effortful saliva swallowing	$\chi^2(2) = 0.00, p = 1.00$
	Effortful 10 mL water swallowing	$\chi^2(2) = 1.00, p = 0.74$
	Non-effortful saliva swallowing	$\chi^2(2) = 0.33, p = 0.95$
	Non-effortful 10 mL water swallowing	$\chi^2(2) = 2.33, p = 0.43$
Time duration between onset	Effortful saliva swallowing	$\chi^2(2) = 0.33, p = 0.95$

of the upper pharynx pressure activity (sensor 1) to the onset of the UES pressure activity (sensor 3)	Effortful 10 mL water swallowing	$\chi^2(2) = 2.33, p = 0.43$
	Non-effortful saliva swallowing	$\chi^2(2) = 4.00, p = 0.18$
	Non-effortful 10 mL water swallowing	$\chi^2(2) = 3.26, p = 0.29$

6.2.1.6 Summary: Pharyngeal pressures events – 4-week training

Friedman's ANOVAs for related means were conducted for data derived from SKL training to investigate differences following 4 weeks of training. There was a significant time effect for sensor 2 duration in non-effortful 10 mL (baseline < post 2 weeks, post 2 weeks < post 4 weeks). However, post hoc analyses revealed only a marginally significant difference between baseline and post 4 weeks. There was a significant time effect for sensor 2 duration in effortful 10 mL swallowing (baseline < post 2 weeks, post 2 weeks < post 4 weeks, post 4 weeks > baseline). However, post hoc analyses revealed non-significant differences. For peak pressure amplitude and relative time durations there were no significant changes. In addition, there were marginally significant effects of time on sensor 3 (UES) duration in non-effortful task, with an increase in duration over time.

6.2.2 Hyoid movement

6.2.2.1 Hyoid movement – 2-week training

Data were available for all (n = 20) of the STR group, all (n = 10) the SKL-I group and nine of the SKL-D group. Missing data (n = 1) was due to difficulty swallowing with the mouth-piece in place.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (hyoid movement) between baseline and post 2-week training (post-training value *minus* baseline value) (STR: 10 old and 10 young, 10 females and 10 males; SKL: 9 old and 10 young, 9 females and 10 males) (Table 6.32). There was a significant effect of GENDER ($F(1, 31) = 4.22, p = 0.049$). The mean difference between Males and Females was -2.40% ($CI [-0.02, -4.78]$, Cohen's $d = 0.70$).

Post hoc analyses were conducted to evaluate the change in hyoid movement following training within each gender, using a paired-sample t-test for males and females separately. For males, there was a significant decrease in hyoid movement from 24.5% ($SD 4.4$) to 23.1% ($SD 4.6$) with

a mean difference of 1.4% ($CI [-2.5, -0.3]$, $t(19) = 2.57$, $p = 0.02$). For females, there was a non-significant effect of training on hyoid movement (mean difference 0.9% increase from baseline to post training ($CI [-1.1, 3.0]$, $t(18) = 0.98$, $p = 0.34$). Since males had a significant reduction, additional analyses were conducted to test if there was a difference between Males in SKL and Males in STR training using a paired-samples t-test. For Males in SKL training, there was a significant decreased in hyoid movement from 24.9% ($SD 4.8$) to 22.7% ($SD 5.1$) with a mean difference of 2.2% ($CI [-3.2, 1.3]$, $t(9) = 5.33$, $p < 0.001$). For Males in STR training, there was no significant effect of training on hyoid movement (baseline: 24.0% ($SD 4.2$), outcome: 23.5% ($SD 4.2$), mean difference: 0.53%, $CI [-2.6, 1.6]$, $t(9) = 0.56$, $p = 0.58$).

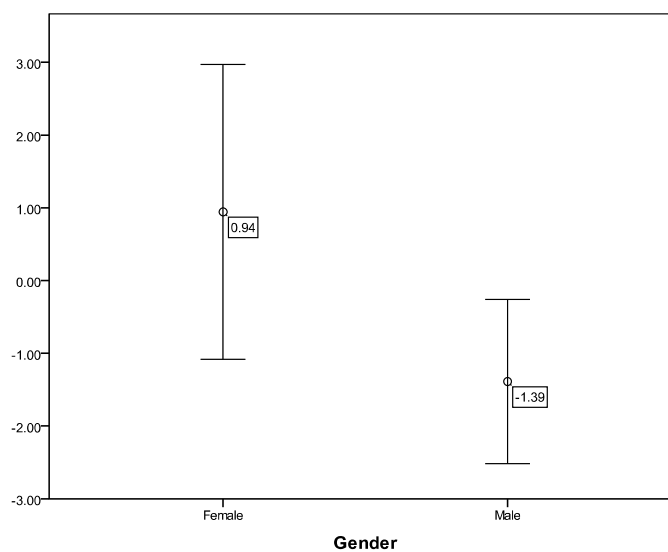


Figure 6.46 Hyoid movement (percentage change): mean difference (post training minus baseline) in percent change from rest to maximum position and 95% CI around the mean, by gender.

In SKL, the estimated mean difference was of 0.89% ($SD 3.6$, $CI [-2.63, 0.85]$, Cohen's $d = 0.19$) decrease from baseline to post-training. In STR, the mean difference was of 0.46% ($SD 3.4$, $CI [-1.16, 2.08]$, Cohen's $d = 0.10$) increase from baseline to post-training.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (hyoid movement) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I: 5 young and 5 old, 5 females and 5 males; SKL-D: 5 young and 4 old, 4 females and 5 males). There were no significant effects (Table 6.32).

Summary: Hyoid movement – 2-week training

To summarize, there were no significant effects of training type when comparing SKL to STR and SKL-I to SKL-D on hyoid movement. There was a significant effect of GENDER ($p = 0.049$, $d = 0.70$). At the group level, Females had an increase whereas Males had decreased hyoid movement following training, regardless of training group. However, additional analysis revealed that following SKL training Males had significantly reduced hyoid movement, but Males in STR did not.

Table 6.32 Factors, F (df), p value: Training effects on hyoid movement (significant results are in bold)

Comparison	Factors, F (df), p value
SKL vs. STR	TRAINING ($F(1, 31) = 1.34, p = 0.26$) GENDER ($F(1, 31) = 4.22, p = 0.049$) AGE ($F(1, 31) = 0.03, p = 0.85$) TRAINING*GENDER ($F(1, 31) = 0.12, p = 0.72$) TRAINING*AGE ($F(1, 31) = 0.14, p = 0.71$) GENDER*AGE ($F(1, 31) = 0.60, p = 0.44$) TRAINING*AGE*GENDER ($F(1, 31) = 0.41, p = 0.53$)
SKL-D vs. SKL-I	TRAINING ($F(1, 15) = 0.13, p = 0.72$) GENDER ($F(1, 15) = 2.67, p = 0.12$) AGE ($F(1, 15) = 0.16, p = 0.70$)

6.2.2.2 Four-week training

Data were available for 9 of the 10 participants. Missing data ($n = 1$) was due to difficulty swallowing with the mouth-piece in place. Due to low number of participants, SKL subgroups were analyzed together as one group ($n = 6$), using Friedman's ANOVAs (non-parametric) for related means (baseline, post 2-week training and post 4-week training). STR group were not analyzed since it consisted on three participants only. Data (percent change relative to baseline) for all subjects is presented in Figure 6.47. In SKL, there was no significant difference between the three time points ($\chi^2(2) = 2.33, p = 0.43$).

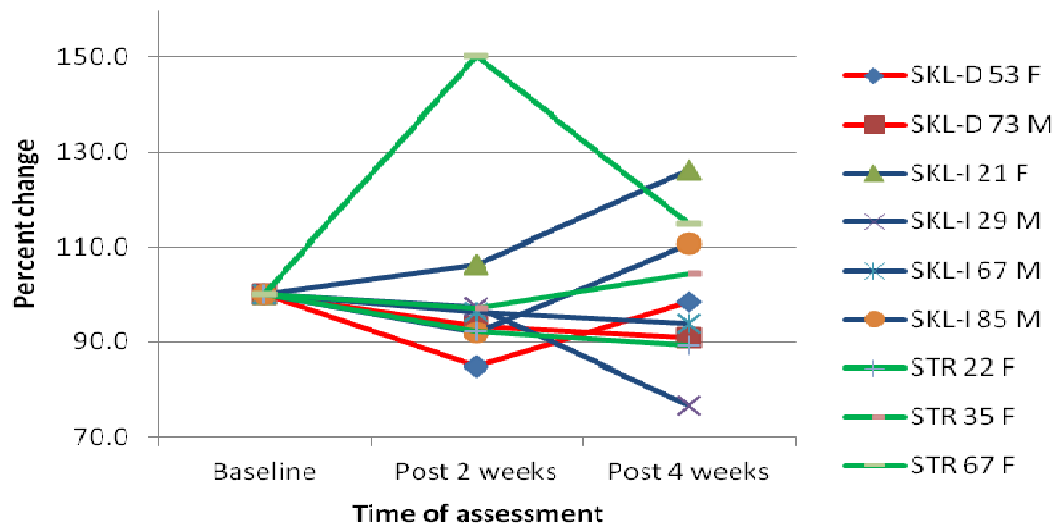


Figure 6.47 Changes over time (baseline, post 2 weeks, post 4 weeks) in hyoid movement (calculated percent change from rest to maximum excursion). Data is presented as percent change from baseline measures (100%).

Summary: Hyoid movement – 4-week training

To summarize, Friedman's ANOVA for related mean was conducted in SKL comparing baseline, 2-week and 4-week measures, but not in STR. No significant differences were found. The changes at post 4 weeks relatively to baseline varied from 75 % to 125 %. No clear trend by group can be described.

6.2.3 Activation of the submental muscle group

6.2.3.1 Submental activation – 2-week training

Data were available for all subjects in both training groups.

Submental muscle activity during effortful saliva swallowing task

Factorial ANOVA was contracted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (sEMG peak amplitude in effortful saliva swallowing) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.37, p. 261). There was a significant effect of TRAINING ($F(1, 32) = 15.42, p < 0.001$). The mean difference was $70.4 \mu V$ ($CI [33.9, 106.9]$, Cohen's $d = 1.11$, STR > SKL) (Figure 6.48).

In SKL, the estimated mean difference was of 0.8 μV (SD 53.6, CI [-25.3, 26.8]) *increase* from baseline to post 2-week training ($t(19) = 0.46$, $p = 0.65$). In STR, the estimated mean difference was of 71.2 μV (SD 66.6, CI [45.6, 96.8]) *increase* from baseline to post 2-week training ($t(19) = 4.78$, $p < 0.001$). Effect sizes are presented in Table 6.36.

There was also a significant effect of AGE ($F(1, 32) = 4.78$, $p = 0.036$). The mean difference was 39.2 μV (CI [2.7, 75.7], Cohen's $d = 0.65$) (Figure 6.49). In Young participants, there was a mean *increase* of 59.2 μV (SD 86.8, CI [18.6, 99.8], $t(19) = 3.05$, $p = 0.01$) from baseline to post 2-week training. In Old participants, there was a mean difference of 17.6 μV (SD 33.7, CI [1.8, 33.4], $t(19) = 2.33$, $p = 0.03$) *increase* from baseline to post 2-week training. Table 6.33 presents the sEMG values at baseline and post-training for each age group, with percent change and effect sizes.

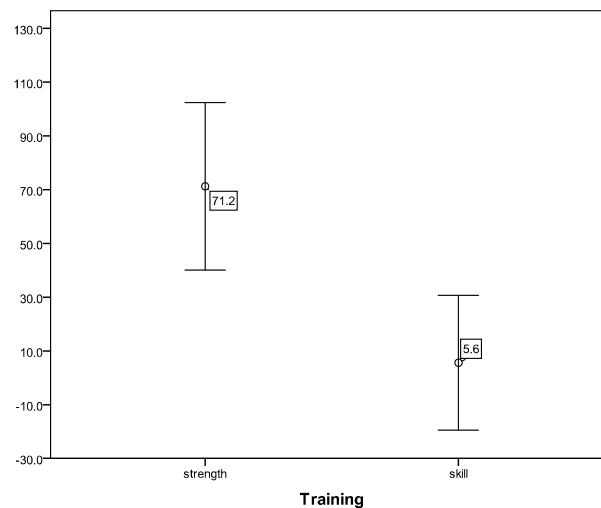


Figure 6.48 sEMG peak amplitude (μV) for effortful saliva swallowing: mean difference (post-training minus baseline) by training type.

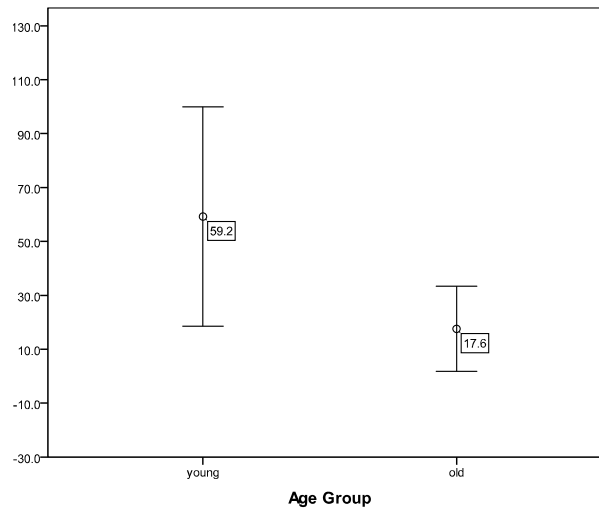


Figure 6.49 sEMG peak amplitude (μV) for effortful saliva swallowing: mean difference (post-training minus baseline) by age group.

Table 6.33 sEMG peak amplitude for effortful saliva swallowing: Estimated marginal means and (SD) for each age group, at baseline and post-training, with percent change relative to baseline and effect size

Age group	Baseline	Outcome	Percent change	Cohen's <i>d</i>
Old	106.3 (42.1)	122.7 (28.1)	115	0.46
Young	156.7 (89.2)	212.3 (101.9)	135	0.60

Additional analyses were conducted to explore the effects of training in the younger and older groups in STR and in SKL, using paired t-tests. In STR, Young had a significant increase ($t(9) = 4.14$, $p = 0.003$) and Old had a significant increase as well ($t(9) = 5.26$, $p = 0.001$). In SKL, Young ($t(9) = 0.63$, $p = 0.54$) and Old ($t(9) = 0.27$, $p = 0.79$) had no significant changes.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (sEMG peak amplitude in effortful saliva swallowing) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.38, p. 262).

Submental muscle activity during effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (sEMG peak amplitude in effortful 10 mL water swallowing) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.37, p. 261).

There was a significant effect of TRAINING ($F(1, 32) = 9.8, p = 0.004$, Cohen's $d = 1.10$) (Figure 6.50). The mean difference in sEMG peak amplitude from baseline to post training, between the training groups was of $55.0 \mu V$ ($CI [19.2, 90.8]$). The effect of TRAINING was investigated using post hoc analysis in each group separately (SKL and STR) using paired t-test with baseline vs. post 2-week training sEMG peak amplitude. In STR, there was a significant effect of training. There was an increase of $60.4 \mu V$ from baseline to post 2-week training ($SD 55.6$; $CI [35.2, 85.6]$, $t(19) = 4.86, p < 0.001$). In SKL, there was no significant effect of training ($t(19) = 0.58, p = 0.56$) with a mean increase of $7.2 \mu V$ from baseline to post 2-week training ($SD 54.8$; $CI [-18.5, 32.8]$).

There was a marginally significant effect of AGE ($p = 0.07, d = 0.66$), with younger subjects having a larger increase than older (Figure 6.51). Table 6.34 presents the sEMG values at baseline and post-training for each age group, with percent change and effect sizes.

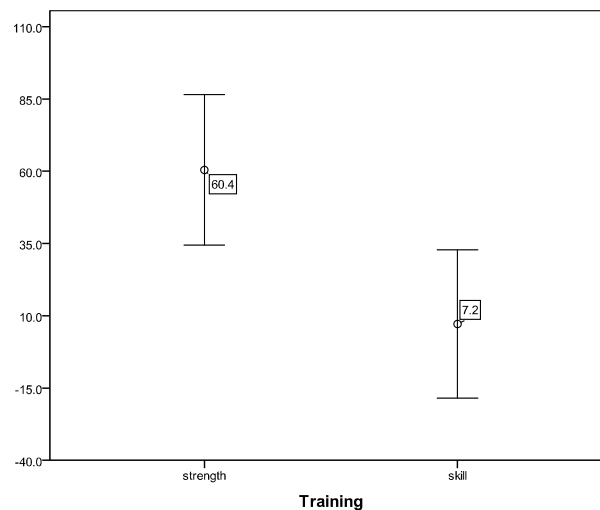


Figure 6.50 sEMG peak amplitude (μV) for effortful 10 mL water swallowing: mean difference (post-training minus baseline) by training type.

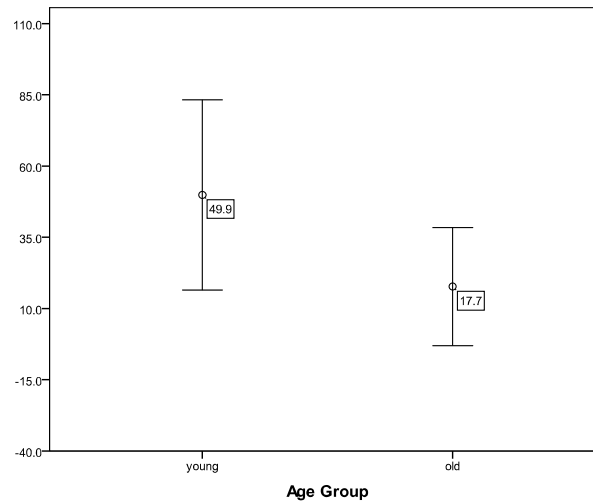


Figure 6.51 sEMG peak amplitude (μV) for effortful 10 mL water swallowing: mean difference (post-training minus baseline) by age group.

Table 6.34 sEMG peak amplitude for effortful 10 mL swallowing: Estimated marginal means and (SD) for each age group, at baseline and post-training, with percent change relative to baseline and effect size

Age group	Baseline	Outcome	Percent change	Cohen's <i>d</i>
Old	101.8 (44.2)	118.3 (28.7)	116	0.44
Young	142.4 (92.4)	191.8 (91.3)	134	0.55

Additional analyses were conducted to explore the effects of training on Young and Old in STR and SKL, using a paired-samples t-test. In STR, Young had a significant increase ($t(9) = 3.67, p = 0.005$), and Old too ($t(9) = 3.82, p = 0.004$). In SKL, Young ($t(9) = 1.02, p = 0.33$) and Old ($t(9) = 0.55, p = 0.59$) had no significant changes.

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (sEMG peak amplitude in effortful 10 mL water swallowing) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.38, p. 262). There was a marginally significant effect TRAINING ($F(1, 16) = 3.97, p = 0.064$, Cohen's $d = 0.95$) (Figure 6.52). In SKL-I there was an estimated mean difference of 15.7 μV decrease from baseline to post 2-week training ($SD 56.0, CI [-50.2, 18.7]$). In SKL-D there was an estimated mean difference of 30.1 μV increase from baseline to post 2-week training ($SD 45.0, CI [-4.4, 64.5]$).

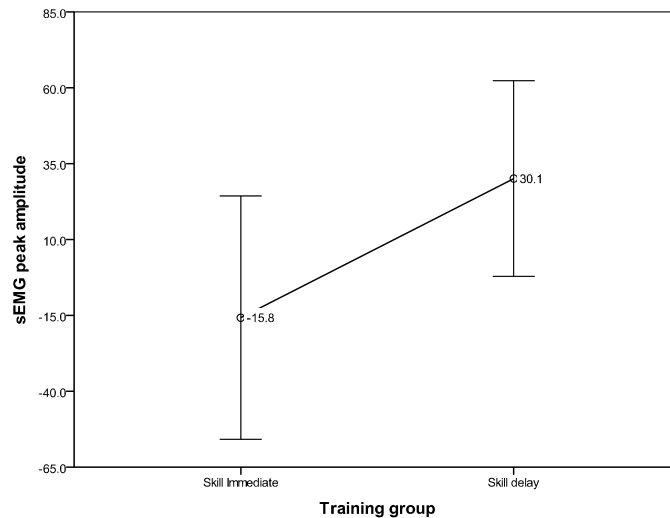


Figure 6.52 sEMG peak amplitude (μV) for effortful 10 mL water swallowing: mean difference (post-training minus baseline) by training group (SKL-I and SKL-D).

Submental muscle activity during non-effortful saliva swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (sEMG peak amplitude in non-effortful saliva swallowing) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.37, p. 261).

In SKL, the estimated mean difference was of 12.5 μV (SD 25.6, CI [-2.8, 27.8]) *increase* from baseline to post-training. In STR, the mean difference was of 3.5 μV (SD 37.3, CI [-11.5, 18.6]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.36.

Additional analyses were conducted to explore the effects of training on Young and Old in STR and SKL, using paired-samples t-tests. In STR, Young ($t(9) = 0.32$, $p = 0.76$) and Old ($t(9) = 0.36$, $p = 0.72$) had no significant changes. In SKL, Young had a marginally significant increase of 21.5 μV (SD 31.2, CI [-0.9, 43.8], $t(9) = 2.17$, $p = 0.058$). Old had no significant change ($t(9) = 0.09$, $p = 0.92$).

Factorial ANOVA that examined the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (sEMG peak amplitude in non-effortful saliva swallowing) between baseline and post 2-week training (post-training value *minus* baseline value), was conducted. There were no significant effects (Table 6.38, p. 262).

There was a marginally significant effect of AGE ($F(1, 16) = 3.63$, $p = 0.075$, Cohen's $d = 0.97$) (Figure 6.53). Old participants produced an estimated mean difference of 0.04 μV decrease from

baseline to post 2-week training (SD 12.9, CI [-17.1, 17.1]). Young participants had an estimated mean difference of 21.9 μV increase from baseline to post 2-week training (SD 31.2, CI [4.8, 39.0]).

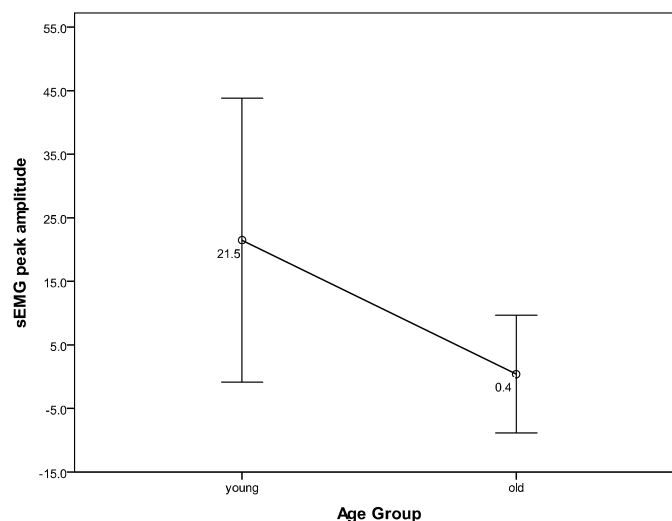


Figure 6.53 sEMG peak amplitude (μV) for non-effortful saliva swallowing: mean difference (post-training minus baseline) by age group.

Submental muscle activity during non-effortful 10 mL water swallowing task

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (sEMG peak amplitude in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value). There were no significant effects (Table 6.37, p. 261).

The effect of AGE was approaching significance ($F(1, 32) = 3.27$, $p = 0.08$, Cohen's $d = 0.65$) (Figure 6.54). Table 6.35 presents the sEMG values at baseline and post-training for each age group, with percent change and effect sizes. In SKL, the estimated mean difference was of 5.0 μV (SD 21.1, CI [-4.7, 14.8]) *increase* from baseline to post-training. In STR, the mean difference was of 4.5 μV (SD 21.1, CI [-5.1, 14.1]) *increase* from baseline to post-training. Effects sizes are reported in Table 6.36.

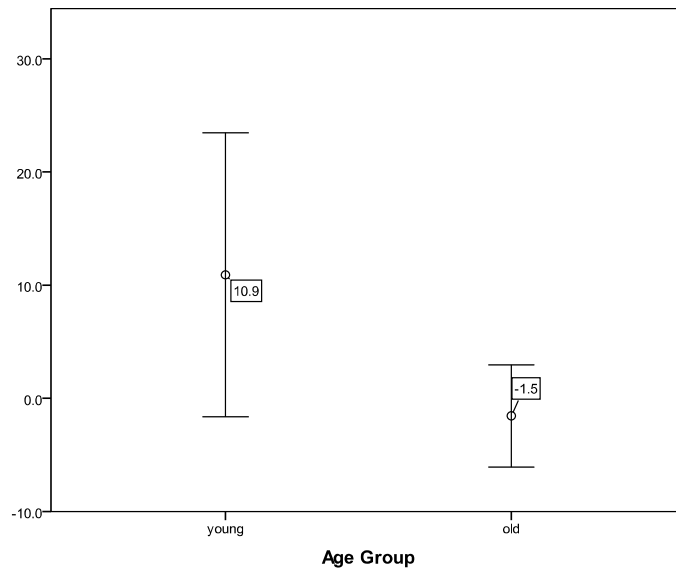


Figure 6.54 sEMG peak amplitude (μV) for non-effortful 10 mL water swallowing: mean difference (post-training minus baseline) by age group.

Table 6.35 sEMG peak amplitude for non-effortful 10 mL swallowing: Estimated marginal means and (SD) for each age group, at baseline and post-training, with percent change relative to baseline and effect size

Age group	Baseline	Outcome	Percent change	Cohen's <i>d</i>
Old	32.9 (15.3)	31.6 (14.6)	96	0.09
Young	48.3 (38.9)	59.2 (37.9)	122	0.29

Additional analyses were conducted to explore the effects of training on Young and Old in STR and SKL, using paired-samples t-tests. In STR, Young ($t(9) = 0.64, p = 0.53$) and Old ($t(9) = 1.06, p = 0.31$) had no significant changes. In SKL, Young had a marginally significant increase of 15.8 μV ($SD\ 24.6, CI\ [-1.7, 33.4], t(9) = 2.04, p = 0.07$). Old had a significant decrease of 6.1 μV ($SD\ 8.2, CI\ [-12.0, -0.3], t(9) = 2.38, p = 0.04$).

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), GENDER, and AGE on the difference in the dependent variable (sEMG peak amplitude in non-effortful 10 mL water swallowing task) between baseline and post 2-week training (post-training value *minus* baseline value) (Table 6.38, p. 262). There was a significant effect of (AGE $F(1, 16) = 5.92, p = 0.03$, Cohen's $d = 1.23$) (Figure 6.55). Old had an estimated mean difference of 5.9 μV decrease from baseline to post 2-week training ($SD\ 8.3, CI\ [-19.0, 7.2]$). Young had an

estimated mean difference of 15.6 μV *increase* from baseline to post 2-week training (SD 24.6, CI [2.5, 28.7]).

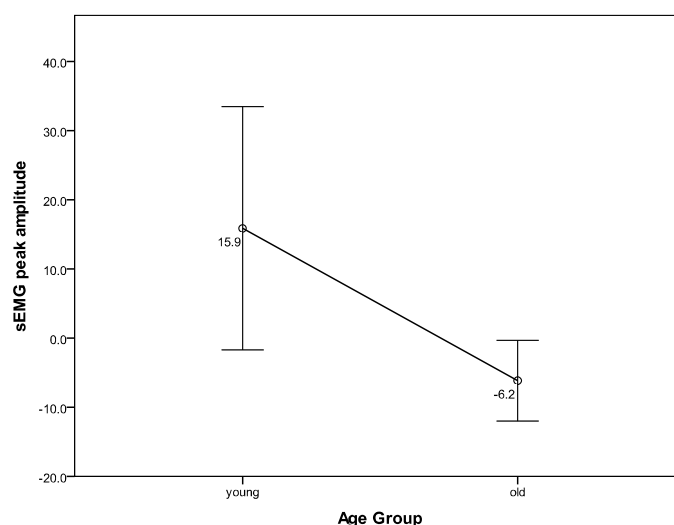


Figure 6.55 sEMG peak amplitude (μV) for non-effortful 10 mL water swallowing: mean difference (post-training minus baseline) by age group.

Table 6.36 Effect size (Cohen's d) for the effect of training group: submental muscle activity

Swallowing task	SKL	STR
Effortful saliva	0.11	0.77
Effortful 10 mL water	0.18	0.65
Non-effortful saliva	0.45	0.10
Non-effortful 10 mL water	0.22	0.10

Summary: Activation of the submental muscle group – 2-week training

During effortful tasks (saliva and water), STR had a larger and statistically significant increase with a large effect size in sEMG peak amplitude, whereas SKL had a small non-significant increase with small effect size. In non-effortful tasks, STR had no effect and SKL had small to medium effects.

In effortful 10 mL water swallowing task there was marginally significant effect of training, with SKL-I training having decrease and SKL-D training having an increase in sEMG peak amplitude following training.

Age had a significant in effortful saliva, and marginally significant effects in effortful water, non-effortful saliva, and for non-effortful water swallowing task. In all four tasks the data indicated that the same trend existed, with Young having a larger increase in sEMG peak amplitude following training (both SKL and STR), than Older subjects. Young subjects had a larger effect size and a larger percent change than Older subjects.

Table 6.37 Factors effects (*F*, *df*, *p* values): Training type (SKL vs. STR), gender, and age group (Young vs. Old): sEMG peak amplitude in 4 swallowing tasks (significant results in bold)

Swallowing task	Factors, <i>F</i> (df), <i>p</i> value
Effortful swallowing – saliva	TRAINING $F(1, 32) = 15.42, p < 0.001$ GENDER $F(1, 32) = 0.17, p = 0.67$ AGE $F(1, 32) = 4.78, p = 0.036$ TRAINING*GENDER $F(1, 32) = 0.84, p = 0.36$ TRAINING*AGE $F(1, 32) = 2.34, p = 0.13$ GENDER*AGE $F(1, 32) = 1.23, p = 0.27$ TRAINING*AGE*GENDER $F(1, 32) = 2.46, p = 0.12$
Effortful swallowing – 10 mL water	TRAINING $F(1, 32) = 9.8, p = 0.004$ GENDER $F(1, 32) = 0.26, p = 0.61$ AGE $F(1, 32) = 3.51, p = 0.07$ TRAINING *GENDER $F(1, 32) = 0.88, p = 0.35$ TRAINING*AGE $F(1, 32) = 0.03, p = 0.85$ GENDER*AGE $F(1, 32) = 0.07, p = 0.79$ TRAINING* AGE*GENDER $F(1, 32) = 1.56, p = 0.22$
Non-effortful swallowing – saliva	TRAINING $F(1, 32) = 0.72, p = 0.40$ GENDER $F(1, 32) = 0.19, p = 0.66$ AGE $F(1, 32) = 1.43, p = 0.24$ TRAINING*GENDER $F(1, 32) = 0.001, p = 0.97$ TRAINING*AGE $F(1, 32) = 0.78, p = 0.38$ GENDER*AGE $F(1, 32) = 0.14, p = 0.71$ TRAINING*AGE*GENDER $F(1, 32) = 1.28, p = 0.26$
Non-effortful swallowing – 10 mL water	TRAINING $F(1, 32) = 0.01, p = 0.93$ GENDER $F(1, 32) = 0.03, p = 0.86$ AGE $F(1, 32) = 3.27, p = 0.08$ TRAINING* GENDER $F(1, 32) = 0.04, p = 0.84$ TRAINING*AGE $F(1, 32) = 0.190, p = 0.17$ GENDER*AGE $F(1, 32) = 0.07, p = 0.78$ TRAINING *AGE*GENDER $F(1, 32) = 0.32, p = 0.57$

Table 6.38 Factors effects (F , df , p values): Training type (SKL-I vs. SKL-D), gender, and age group (Young vs. Old): sEMG peak amplitude in 4 swallowing tasks (significant results are in bold)

Swallowing task	Factors, F (df), p value
Effortful swallowing – saliva	TRAINING $F(1, 16) = 1.36, p = 0.26$ GENDER $F(1, 16) = 0.95, p = 0.34$ AGE $F(1, 16) = 0.29, p = 0.64$
Effortful swallowing - 10 mL water	TRAINING $F(1, 16) = 3.97, p = 0.064$ GENDER $F(1, 16) = 0.10, p = 0.75$ AGE $F(1, 16) = 1.59, p = 0.22$
Non-effortful swallowing - saliva	TRAINING $F(1, 16) = 0.00, p = 0.98$ GENDER $F(1, 16) = 0.14, p = 0.71$ AGE $F(1, 16) = 3.63, p = 0.075$
Non-effortful swallowing - 10 mL water	TRAINING $F(1, 16) = 0.01, p = 0.92$ GENDER $F(1, 16) = 0.08, p = 0.78$ AGE $F(1, 16) = 5.92, p = 0.03$

6.2.3.2 Submental activation – 4-week training

One subject had missing data for the effortful tasks (saliva and 10 mL water) at post 4-week training assessment due to peak clipping at 200 μ V. Thus, data is presented for 9/10 participants in the effortful swallowing tasks and 10/10 in the non-effortful swallowing tasks. The data below represent the percentage of change in peak amplitude from baseline (100%) to post 2-week training and from baseline to post 4-week training, for each subject.

Due to low number of participants, SKL subgroups were analyzed together ($n = 7$), as one group using Friedman's ANOVAs (non-parametric) for related means (pre-training, post 2-week training and post 4-week training) (Table 6.39). There were no significant effects of training. STR group was not analyzed. The raw data is presented in Appendix 8.

Table 6.39 Friedman's ANOVA: sEMG peak amplitude – 4-week protocol, in SKL (n = 7)

Task	Friedman's ANOVA result
Effortful saliva swallowing	$\chi^2(2) = 0.28, p = 0.96$
Effortful 10 mL water swallowing	$\chi^2(2) = 2.57, p = 0.30$
Non-effortful saliva swallowing	$\chi^2(2) = 2.57, p = 0.30$
Non-effortful 10 mL water swallowing	$\chi^2(2) = 0.28, p = 0.96$

Percentage change in peak amplitude is presented in Figure 6.56 for effortful saliva swallowing and Figure 6.57 for effortful 10 mL water swallowing. Percentage change in peak amplitude is presented in Figure 6.58 for non-effortful saliva swallowing and Figure 6.59 for non-effortful 10 mL water swallowing.

STR 21 F had an increase in sEMG peak amplitude in all swallowing tasks. During effortful tasks, STR 22 F had an increase in peak amplitude. STR 67 F had an increase during effortful water swallowing task.

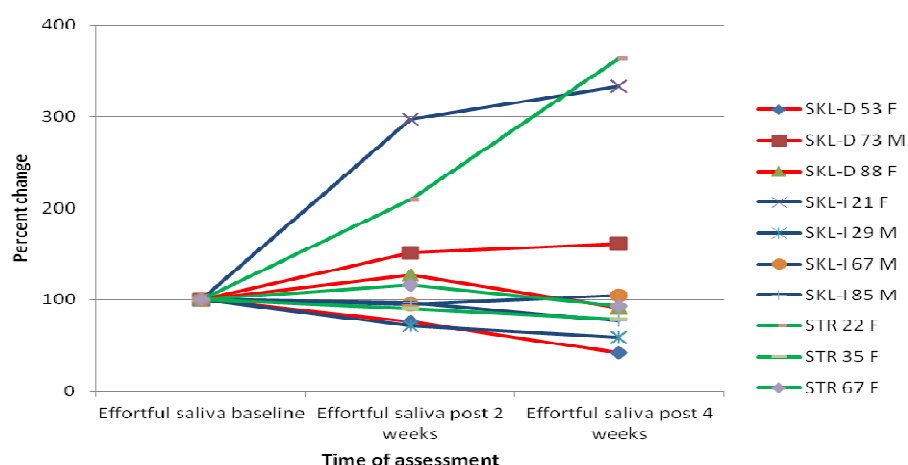


Figure 6.56 Percentage of change in mean of sEMG peak amplitude from baseline to post 2-week training and to post 4-week training, during effortful saliva swallowing task, for each participant in the 4-week protocol.

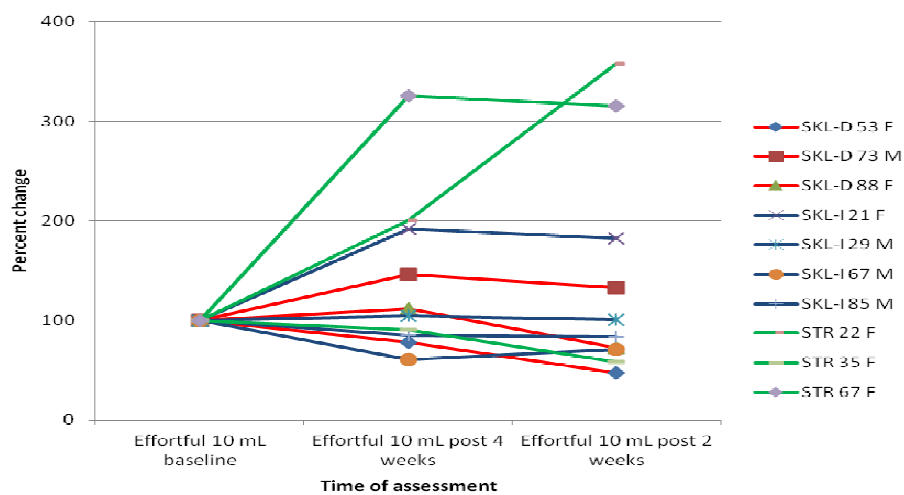


Figure 6.57 Percentage of change in mean of sEMG peak amplitude from baseline to post 2-week training and to post 4-week training, during effortful 10 mL water swallowing task for each participant in the 4-week protocol.

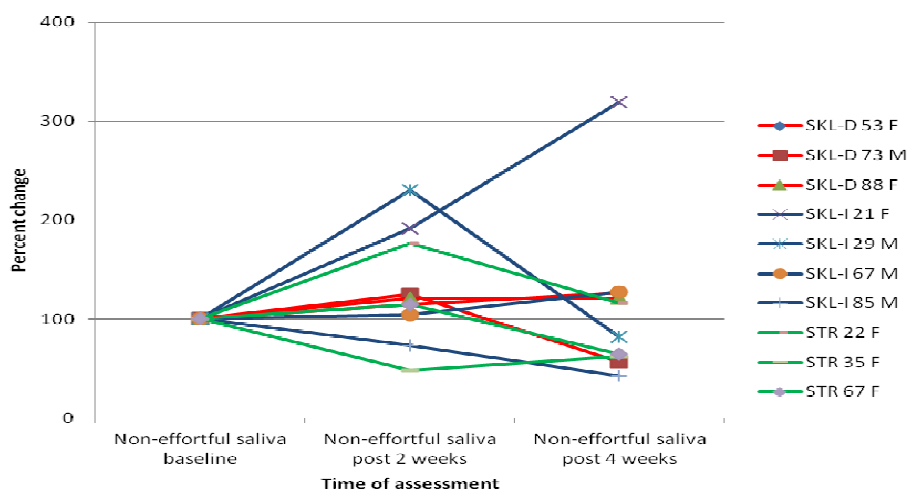


Figure 6.58 Percentage of change in mean of sEMG peak amplitude from baseline to post 2-week training and to post 4-week training, during non-effortful saliva swallowing task, for each participant in the 4-week protocol.

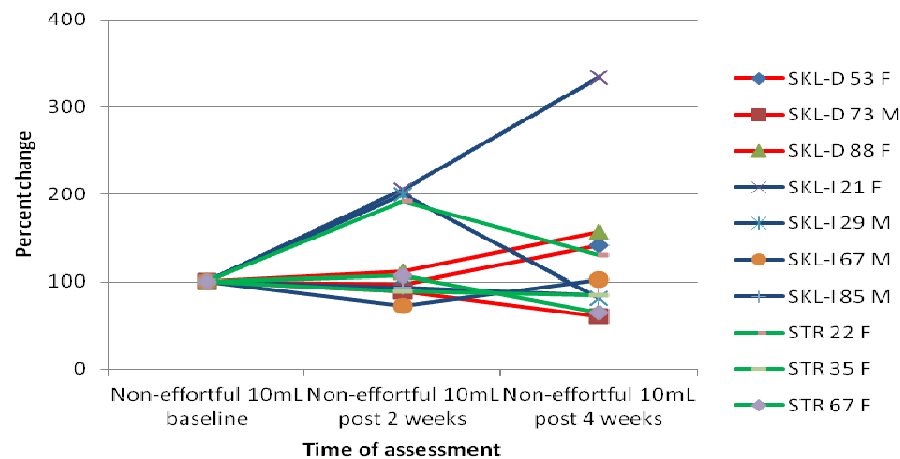


Figure 6.59 *Percentage of change in mean of sEMG peak amplitude from baseline to post 2-week training and to post 4-week training, during non-effortful 10 mL swallowing task for each participant in the 4-week protocol.*

Summary: Activation of the submental muscle group – 4-week training

To summarize, Friedman's ANOVAs for related mean were conducted on the results of SKL training comparing baseline, 2-week and 4-week measures. No significant differences were found. Due to the small sample size in the STR group, descriptive statistics were used, and trends were described, with no implication of statistical significance. The rest of the subjects had changes ranging from 50% to 150% from baseline to *post 4-week training*.

6.3 Structural muscle changes

Six subjects had missing data due to technical difficulties. Equipment quality restricted visibility when excessive fat tissue was present. Subjects for whom data was entered into the model are specified below. The CSA of right and left anterior belly of digastric was averaged. Data for geniohyoid could not be analyzed due to reduced data quality.

6.3.1 Anterior belly of digastric – 2-week training

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL vs. STR), GENDER, and AGE on the difference in the dependent variable (CSA of anterior belly of digastric) between baseline and post 2-week training (post-training value *minus* baseline value) (STR: n = 17, 9 young and 8 old, 10 females and 7 males; SKL: n = 17, 10 young and 7 old, 10 females and 7 males). There were no significant effects (Table 6.40).

In SKL, the estimated mean difference was of 0.05 cm² *increase* (*SD* 0.16, *CI* [-0.04, 0.13], Cohen's *d* = 0.14) from baseline to post 2-week training. In STR, the estimated mean difference was of 0.05 cm² *decrease* from baseline to post 2-week training (*SD* 0.14; *CI* [-0.13, 0.03], Cohen's *d* = 0.17).

Factorial ANOVA was conducted to examine the effects of TRAINING (SKL-I vs. SKL-D), and GENDER, and AGE on the difference in the dependent variable (CSA of anterior belly of digastric) between baseline and post 2-week training (post-training value *minus* baseline value) (SKL-I: 5 old and 5 young; SKL-D 2 old and 5 young). There were no significant effects (Table 6.40).

Summary: Anterior belly of digastric CSA – 2-week training

To summarize, there were no differences between training groups when comparing SKL to STR, and SKL-I to SKL-D.

Table 6.40 Factors, F (df), p value: training type, age and gender effects on CSA of anterior digastric (significant results are in bold)

Comparison	Factors, F (df), p value
SKL vs. STR	<p>TRAINING $F(1, 26) = 3.20, p = 0.085$</p> <p>GENDER $F(1, 26) = 0.38, p = 0.54$</p> <p>AGE $F(1, 26) = 1.05, p = 0.31$</p> <p>TRAINING*GENDER $F(1, 26) = 0.57, p = 0.46$</p> <p>TRAINING*AGE $F(1, 26) = 0.23, p = 0.63$</p> <p>GENDER*AGE $F(1, 26) = 0.01, p = 0.90$</p> <p>TRAINING*AGE*GENDER $F(1, 26) = 0.31, p = 0.57$</p>
SKL-I vs. SKL-D	<p>TRAINING $F(1, 13) = 0.24, p = 0.63$</p> <p>GENDER $F(1, 13) = 0.00, p = 0.98$</p> <p>AGE $F(1, 13) = 0.08, p = 0.78$</p>

6.3.2 Anterior belly of digastric – 4-week training

Data were available for 9 out of the 10 participants that took part in this pilot study. Due to the small sample size, SKL subgroups were analyzed as one group using non-parametric Friedman's ANOVAs for related means (pre-training, post 2-week training and post 4-week training) to investigate differences over time. STR group data was not analyzed since only three subjects were included. In SKL (*n* = 6) there was no significant difference between the three time points ($\chi^2(2) = 1.33, p = 0.57$).

Changes in CSA over time (baseline, post 2-week training, and post 4-week training) are presented in Figure 6.60 as percent change from baseline (100%) to post 2-week training and to post 4-week training for each subject.

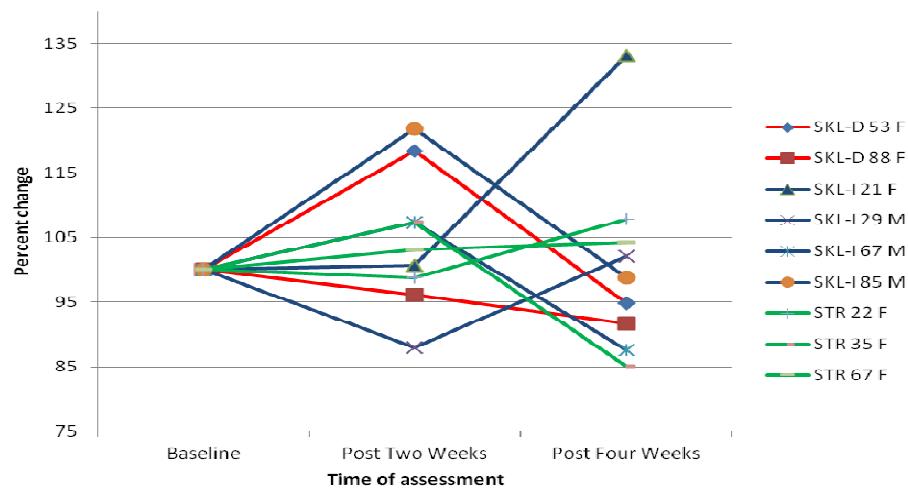


Figure 6.60 Percent change in CSA (cm²) of anterior belly of digastrics (average of right and left) from baseline to post 2-week training and to post 4-week training.

Summary: Anterior belly of digastric CSA – 4-week training

To summarize, Friedman's ANOVA for related mean was conducted for data from the SKL training group. No significant differences were found. Other than SKL-I 21 F that had 135% increase from baseline to post 4-week training, all other subjects had changes between 85%-105% from baseline to post 4-week training in the CSA of anterior bellies of digastrics.

6.4 Subjects performance during swallowing training

6.4.1 Performance – 2-week training

6.4.1.1 Target hit rate in skill training

Data were collected for all the participants in the skill training group (SKL-I: 5 young and 5 old; 5 female and 5 male; SKL-D 5 young and 5 old; 5 female and 5 male). This outcome measure is irrelevant for the strength training group, and their performance are reported in 6.4.1.2.

The subjects in SKL-D were introduced to the delayed feedback protocol at session three (see 5.5.1.1), and hence, the score of this session was entered into the analysis to represent the starting point. In order to match this, the same time point (session three) was chosen for the SKL-I group.

To investigate if there were significant changes in hit rate from training session 3 to training session 10, the *change* in hit rate between session 3 to session 10 (session 10 *minus* session 3) was entered as the outcome variable, and TRAINING (SKL-I vs. SKL-D), AGE, and GENDER as factors. Between-groups main effects were investigated, without interactions due to the small group size (Table 6.42).

There was a significant effect of TIME ($F(1, 16) = 8.42, p = 0.01, d = 1.45$) indicating that both SKL subgroups changed their hit-rate over time. The interaction of TIME*TRAINING was not significant ($p = 0.15, d = 0.75$). The mean difference between the groups was 3.0% ($CI [-1.2, 7.2]$). SKL-D had a mean change of 4.4% ($CI [1.4, 7.4]$) increase from the third session to the 10th and SKL-I had a mean change of 1.4% ($CI [-1.6, 4.4]$) increase from the third session to the 10th.

The target hit rate results for each of the 10 sessions are plotted in Figure 6.61 for both groups together ($n = 20$), and in Figure 6.62 for the SKL-I group ($n = 10$) and SKL-D group ($n = 10$). Over all training sessions (1-10), SKL-I had a mean hit rate of 72.0% ($CI [69.9, 74.0]$), and SKL-D had a mean hit rate of 64.7% ($CI [62.6, 66.7]$).

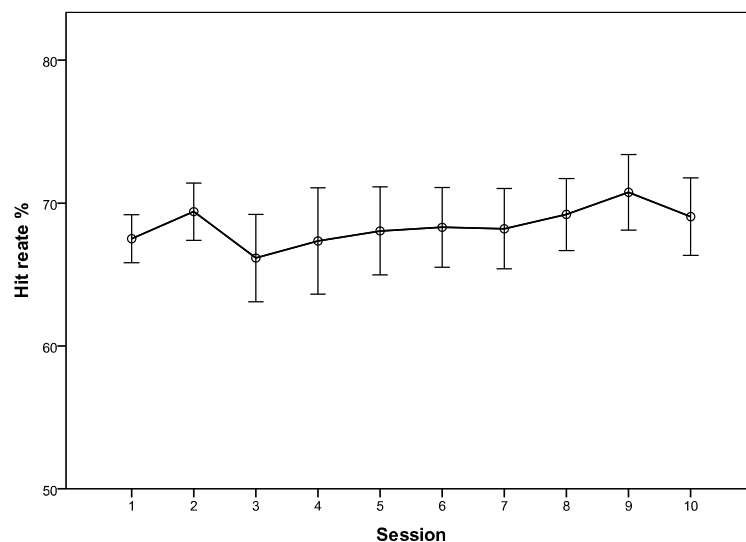


Figure 6.61 Mean hit rate (%) for each training session (1-10), for SKL group. Error bars represent 95% confidence intervals.

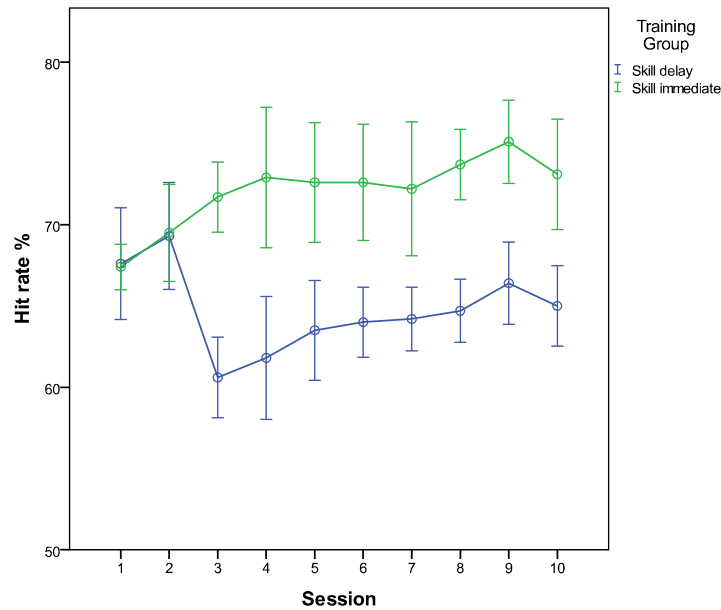


Figure 6.62 Mean hit rate for each training session (1-10), for SKL-I and SKL-D. Error bars represent 95% confidence intervals.

Since there is some evidence to suggest that fast learning and improved performance occur at the initial stages of learning a new motor task (Floyer-Lea & Matthews, 2005; Karni et al., 1995), an additional analysis was conducted. For the SKL-I group the change from session 1 to session 10 was entered into the analysis (session 10 minus session 1) and for SKL-D group the change from session 3 to session 10 was entered. The results were non-significant for the effect of TRAINING ($F(1, 16) = 0.28, p = 0.60$). The mean difference in hit rate between the groups was 1.3% ($CI [-3.8, 6.4]$) (SKL-I > SKL-D).

6.4.1.2 Mean sEMG peak amplitude in strength training

Mixed ANOVA with TIME (training session 1-10), AGE, and GENDER was conducted to investigate whether there were changes in sEMG peak amplitude collected in each training session (the mean peak amplitude for each session was an average of 100 swallows executed in one session) in STR training group (Table 6.42).

There was a significant effect of TIME ($F(4.2, 68.5) = 18.23, p < 0.001$) (Figure 6.63). The difference between the mean sEMG value at the first training session and the value at the last (10th) training session was 43.0 μV ($CI [30.1, 56.1], p < 0.001$).

There was a significant interaction of TIME*AGE ($F(4.2, 68.5) = 4.22, p = 0.003$), presented in Figure 6.64. Young subjects had a greater increase in sEMG peak amplitude over TIME (training sessions) in comparison to Old who had a more moderate increase. The effect of AGE was

significant as well ($F(1, 16) = 12.98, p = 0.002$). The difference between Young and Old was 51.2 μV ($CI [21.1, 81.4]$) (Table 6.41).

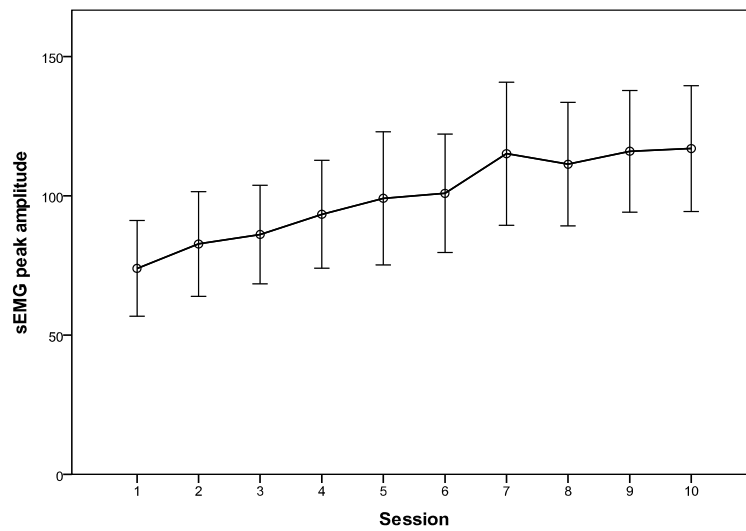


Figure 6.63 Effect of TIME in STR. Mean sEMG peak amplitude collected for each training session (1-10) and 95% confidence intervals around the mean.

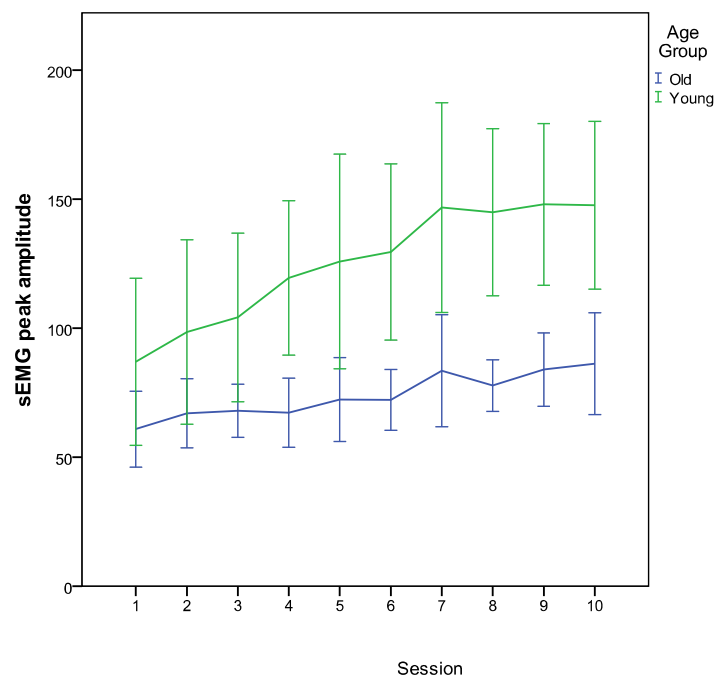


Figure 6.64 Interaction of TIME*AGE in STR. Mean sEMG peak amplitude collected for each training session (1-10) and confidence intervals around the mean.

Table 6.41 Estimated means (predicted means) for the averaged sEMG amplitude (μV) collected in training session 1 – 10, by age group in STR

Age group	Mean	95% Confidence Interval	
		Lower Bound	Upper Bound
Old	73.9	52.6	95.2
Young	125.2	103.8	146.5

6.4.1.3 Summary: Performance – 2-week training

Target hit rate in skill training

There was a significant increase in hit rate from session 3 to session 10 in the SKL training group. There were no significant differences between SKL-I and SKL-D. However, the results indicated a non-significant trend towards a higher hit rate for SKL-D than SKL-I when measuring the difference between session 3 to session 10. Over all training sessions (1-10), SKL-I had a hit rate of 72.0% and SKL-D – 64.7%

Mean sEMG peak amplitude in strength training

Over the course of training, there was a significant increase in the mean submental sEMG value. In addition, Young subjects had a greater sEMG value than Old subjects. The significant interaction of TIME*AGE gives further insight into the effect of AGE, with Young subjects having a greater increase in sEMG peak amplitude over the course of training in comparison to Old subjects who had a more moderate increase.

Table 6.42 Factor effects (F , df , p values): Effects of training type, gender, and age group on training performance: Hit rate and mean sEMG amplitude, collected during every training session (1-10) (significant results are in bold)

Outcome measure	Training groups included	Factors, F (df), p value
Hit rate	SKL-I vs. SKL-D	TIME $F(1, 16) = 8.42, p = 0.01$ TRAINING $F(1, 16) = 2.25, p = 0.15$ GENDER $F(1, 16) = 0.02, p = 0.88$ AGE $F(1, 16) = 0.05, p = 0.82$
Mean sEMG amplitude during training session	STR	TIME $F(4.2, 68.5) = 18.23, p < 0.001$ TIME*GENDER $F(4.2, 68.5) = 0.75, p = 0.57$ TIME*AGE $F(4.2, 68.5) = 4.22, p = 0.003$

		TIME*GENDER*AGE $F(4.2, 68.5) = 0.66, p = 0.63$ GENDER $F(1, 16) = 1.66, p = 0.21$ AGE $F(1, 16) = 12.99, p = 0.002$
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6.4.2 Performance – 4-week training

6.4.2.1 Target hit rate in skill training

Data were collected for all the participants in the skill training group (SKL-I and SKL-D) that took part in the 4-week training protocol. Their data is presented in Figure 6.65. The arithmetic difference of hit rate between sessions 3-18 (session 18 minus session 3) was calculated. In SKL-I the mean change was 0.5% (SD 3.7) and in SKL-D the mean change was 7.0% (SD 4.6).

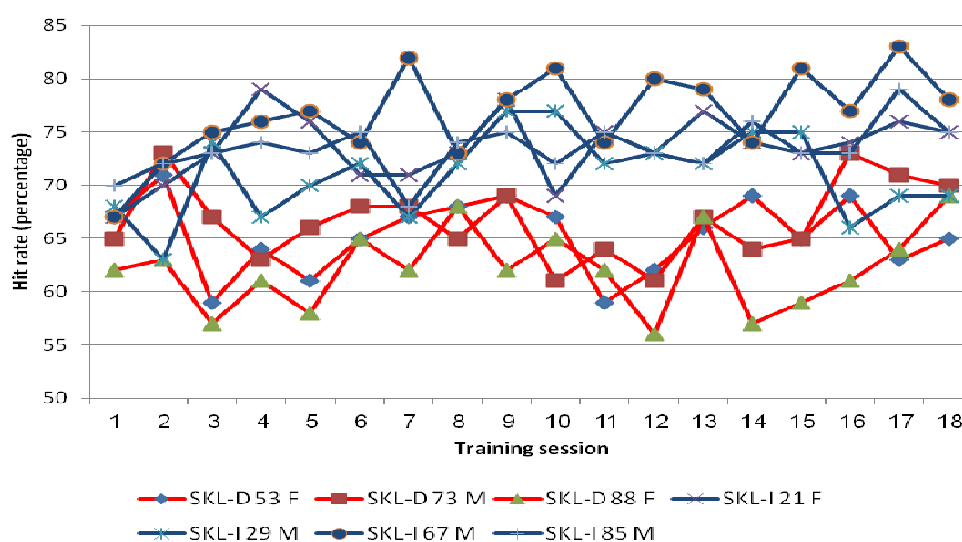


Figure 6.65 Mean of hit rate (percentage) for each training session (1-18), for SKL training subjects on the 4-week training protocol.

6.4.2.2 Mean sEMG peak amplitude during strength training

sEMG peak amplitude was collected for training session 1-18 (the mean peak amplitude for each session was an average of 100 swallows executed in one session). Data was available for all subjects in STR training ($n = 3$) taking part in the 4-week protocol, except for one session for STR-67-F who did not have the data for the last training session (18th) due to computer failure in saving this information. The data are presented graphically in Figure 6.66. STR 22 F is the only subject that seemed to gradually increase the sEMG amplitude over the course of training.

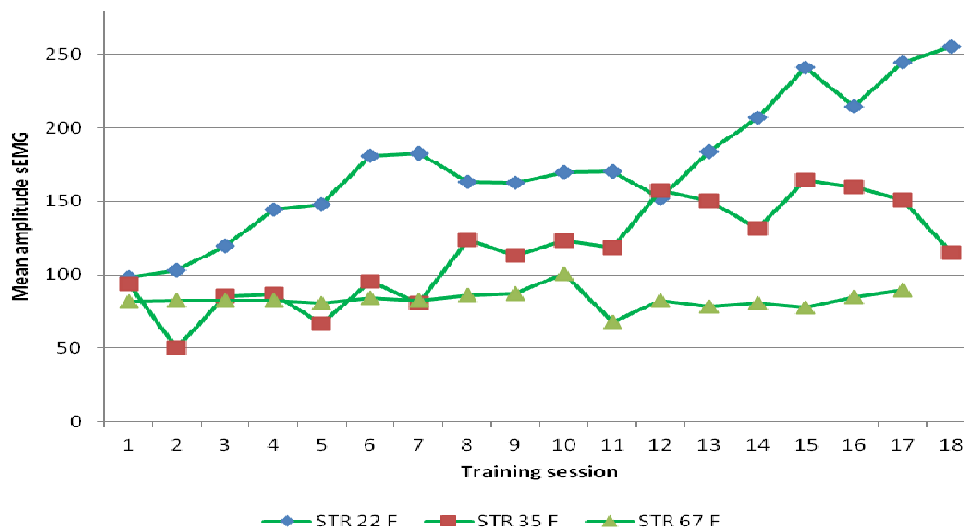


Figure 6.66 Mean sEMG peak amplitude (μV) in each training session (1 – 18) for STR subjects in the 4-week training protocol.

6.4.2.3 Summary: Performance – 4-week training

Target hit rate in skill training

To summarize, SKL-I group members had a small change in hit rate (0.5%), and SKL-D had a relatively large change in hit rate when measuring the change from the 3rd session to the 18th session.

Mean sEMG peak amplitude during strength training

Visual examination of the graphs indicated that the STR group members ($n = 3$) indicated the only one subjects had a higher sEMG peak amplitude at the last session than the first training session.

6.5 Subjective ratings of swallowing training

Data were collected at the end of the training period, thus 26 subjects filled the questionnaires after the 2-week training (missing data $n = 4$), and nine after the 4-weeks training (missing data $n = 1$).

The score (1-5 scale) of each of the 10 questions was averaged. Then, the scores for each of the following four areas were averaged as well: positive questions regarding the experience, negative questions regarding the experience, positive questions regarding swallowing outcomes, and negative questions regarding swallowing outcomes (see Section 5.7.5 for details).

The Kruskal-Wallis test for independent groups (non-parametric) was conducted with TRAINING (SKL-I vs. SKL-D vs. STR) as a factor, and the mean score in each of the four areas as the outcome measure. The analysis was conducted for each of the four question groups (averaged) (A – D) separately. The results were:

A. Positive questions regarding the experience: There was no significant difference between the training group ($H(2) = 3.59, p = 0.16$).

B. Negative questions regarding the experience: There was no significant difference between the training group ($H(2) = 3.35, p = 0.18$).

C. Positive questions regarding swallowing outcomes: There was no significant difference between the training group ($H(2) = 4.41, p = 0.11$).

D. Negative questions regarding swallowing outcomes: There was no significant difference between the training group ($H(2) = 1.43, p = 0.48$).

Table 6.43 presents descriptive statistics for all subjects (main study and extended study), by training group. Table 6.44 presents descriptive statistics for the 2-week training and for the 4-week training protocols.

Table 6.43 Descriptive statistics for the following questions type: positive questions regarding the experience (A), negative questions regarding the experience (B), positive questions regarding swallowing outcomes (C) and negative questions regarding swallowing outcomes (D), by training type

Training group			Question type			
			A	B	C	D
SKL-D	N	Valid	8	8	8	8
		Missing	2	2	2	2
	Mean		4.50	1.56	4.20	1.50
	SE		.16	.23	.15	.22
	SD		.46	.67	.43	.64
	Min		4.00	1.00	3.67	1.00
	Max		5.00	2.50	5.00	2.67
SKL-I	N	Valid	9	9	9	9
		Missing	1	1	1	1
	Mean		4.55	1.38	3.74	1.81
	SE		.22	.20	.23	.21

		<i>SD</i>	.68	.60	.70	.64
		Min	3.50	1.00	3.00	1.00
		Max	5.00	2.50	5.00	3.00
STR	N	Valid	18	18	18	18
		Missing	2	2	2	2
		Mean	4.11	1.97	3.70	1.62
		<i>SE</i>	.16	.21	.12	.13
		<i>SD</i>	.67	.88	.52	.55
		Min	2.50	1.00	2.67	1.00
		Max	5.00	4.00	4.67	2.67

Table 6.44 Descriptive statistics for the following questions type: positive questions regarding the experience (A), negative questions regarding the experience (B), positive questions regarding swallowing outcomes (C) and negative questions regarding swallowing outcomes (D), by training length

Training length			Question type			
			A	B	C	D
2 weeks	N	Valid	26	26	26	26
		Missing	4	4	4	4
		Mean	4.23	1.84	3.76	1.69
		<i>SE</i>	.127	.16	.110	.11
		<i>SD</i>	.65	.83	.56	.58
		Range	2.50	3.00	2.33	1.67
		Min	2.50	1.00	2.67	1.00
		Max	5.00	4.00	5.00	2.67
4 weeks	N	Valid	9	9	9	9
		Missing	1	1	1	1
		Mean	4.55	1.38	4.00	1.51
		<i>SE</i>	.21	.20	.21	.20
		<i>SD</i>	.63	.60	.62	.62
		Range	1.50	1.50	2.00	2.00
		Min	3.50	1.00	3.00	1.00
		Max	5.00	2.50	5.00	3.00

Summary: Swallowing training questionnaire

To summarize, there were no statistically significant differences between the training groups in questionnaire scores. Examination of the data indicated a trend towards SKL-D having slightly higher score for the positive questions regarding swallowing outcome (category C) than the other two groups, and STR had a trend towards slightly higher scores for the negative questions regarding the training experience (category B) than the other two groups. Members of the 4-week training protocol had a trend towards a slightly higher score for the positive questions (category A and C) and a slightly lower score for the negative questions (category B and D) in comparison to the members of the 2-week training protocol.

Table 6.45 Significant (in bold) and marginally significant differences found in the main study: the effects of training type, age group, and gender in swallowing training

<i>Measurement</i>		<i>Statistically significant and marginally significant effects and details</i>
Submental MEP Area	Post 1 st session: contraction task	AGE ($p = 0.053$, $d = 0.95$). Old had a larger MEP area than Young.
	Post 1 st session: swallowing task	NA
	Post 10 th session: contraction task	SKL vs. STR: AGE ($p = 0.006$, $d = 1.39$). Old had a larger MEP area than Young. SKL vs. STR: TRAINING ($p = 0.09$, $d = 0.79$). STR had a larger MEP magnitude than SKL.
	Post 10 th session: swallowing task	SKL vs. STR: AGE ($p = 0.036$, $d = 1.15$). Old had a larger MEP area than Young. SKL vs. STR: GENDER ($p = 0.037$, $d = 1.13$). Females had a larger MEP area than Males.
	Immediate changes: 1 st vs. 10 th session: contraction task	SKL vs. STR: AGE ($p = 0.036$, $d = 1.07$). Old had a larger MEP area than Young.
	Immediate changes: 1 st vs. 10 th session: swallowing task	SKL vs. STR: GENDER ($p = 0.052$, $d = 1.00$). Females had a trend towards larger MEP magnitude than Males.
	Long-term effects: contraction task	SKL vs. STR: TRAINING ($p = 0.07$, $d = 0.79$). STR had a non-significant ($p = 0.11$) <i>increase</i> , whereas SKL had a non-significant <i>decrease</i> ($p = 0.31$) in MEP area following training.
	Long-term effects: swallowing task	NA
Pharyngeal Pressure	Sensor 1 peak	SKL vs. STR: Non-effortful saliva: GENDER*AGE ($p = 0.02$, $d = 0.92$). Old/Females and Young/Males showed greater increase in pressure following training, than Young /Females and Old/Males that showed little change. young males ($p = 0.054$), old females ($p = 0.22$). SKL vs. STR: Non-effortful saliva: TRAINING*GENDER ($p = 0.07$, $d = 0.70$). Females in SKL, Males in STR, and Males in SKL had a trend towards an increase in peak pressure of sensor 1 in non-effortful saliva than Females in STR
	Sensor 2 peak	SKL-I vs. SKL-D: Effortful saliva: TRAINING ($p = 0.01$, $d = 1.62$). SKL-D had decreased peak pressure and SKL-I increased peak pressure. SKL-I vs. SKL-D: Effortful 10 mL: TRAINING ($p = 0.01$, $d = 1.64$). SKL-D had decreased peak pressure and SKL-I increased peak pressure. SKL-I vs. SKL-D: Non-effortful saliva: TRAINING ($p = 0.044$, $d = 1.01$). SKL-D had decreased peak pressure and SKL-I increased peak pressure. SKL-I vs. SKL-D: Non-effortful 10 mL: TRAINING ($p = 0.025$, $d = 1.22$). SKL-D had decreased peak pressure and SKL-I increased peak

	pressure.
Sensor 3 nadir	<p>SKL-I vs. SKL-D: Effortful saliva: AGE ($p = 0.085$, $d = 1.01$). Younger subjects increasing UES pressure and Older decreasing the UES pressure following both types of SKL training.</p> <p>SKL vs. STR: Non-effortful saliva: GENDER ($p = 0.017$, $d = 0.96$) Females had a significant <i>decrease</i> in UES pressure ($p = 0.02$). Males had no change in UES pressure ($p = 0.17$). Females in SKL had a non-significant change in UES pressure ($p = 0.14$). Females in STR had a marginally significant <i>decrease</i> in UES pressure ($p = 0.08$). Males in SKL training had a marginally significant <i>increase</i> in UES pressure ($p = 0.07$).</p> <p>SKL-I vs. SKL-D: Non-effortful saliva: GENDER ($p = 0.048$, $d = 1.12$) Males showed less negativity following training, but Females- increased.</p> <p>SKL vs. STR: Non-effortful 10 mL: TRAINING*GENDER ($p = 0.02$, $d = 0.92$) Males /STR had less negativity following training. However, Females/STR had more negativity. Females and Males in SKL had little change. In SKL, GENDER had no significant effect ($p = 0.98$). In STR, GENDER had a significant effect ($p = 0.003$) with Females having <i>decreased</i> UES pressure following training ($p = 0.03$, $d = 0.86$), and Males having <i>increased</i> UES pressure following training ($p = 0.04$, $d = 0.92$).</p> <p>SKL vs. STR: Non-effortful water: GENDER ($p = 0.060$, $d = 0.79$). Females decreased UES pressure in comparison with Males</p>
Sensor 1 duration	SKL vs. STR: Non-effortful saliva: TRAINING*AGE ($p = 0.052$, $d = 0.74$) Young/STR had shorter duration following training and Old/STR had an increase in duration. In SKL, both Young and Old had an increase
Sensor 2 duration	<p>SKL-I vs. SKL-D: Non-effortful 10 mL: AGE ($p = 0.01$, $d = 1.50$): Older had a larger change (increase) than young following training.</p> <p>SKL-I vs. SKL-D: Non-effortful 10 mL: GENDER ($p = 0.095$, $d = 0.95$). Females had a larger increase following training than males.</p> <p>SKL vs. STR: Effortful 10 mL: AGE ($p = 0.07$, $d = 0.65$). Older had a larger change (increase) than young following training.</p> <p>SKL-I vs. SKL-D: Effortful 10 mL: TRAINING ($p = 0.06$, $d = 0.97$). SKL-I had a large increase. SKL-D had a small decrease.</p>
Sensor 3 duration	<p>SKL vs. STR: Effortful saliva: TRAINING*GENDER ($p = 0.039$, $d = 0.82$) Females in STR, and Males in SKL had a decrease in duration following training, but Males in STR Females in SKL had little change in duration.</p> <p>SKL vs. STR: Effortful saliva: TRAINING*AGE ($p = 0.047$, $d = 0.79$). Old/STR and Young/SKL had a decrease in duration following training, but Young /STR and Old /SKL had little change.</p> <p>SKL vs. STR: Effortful 10 mL: TRAINING*GENDER ($p = 0.03$, $d = 0.84$). In SKL, Males had a decrease ($p = 0.02$) in duration following training, but Females - an increase ($p = 0.12$). In STR, both Females and Males had little change.</p> <p>SKL vs. STR: Effortful 10 mL: GENDER ($p = 0.02$, $d = 0.90$). Males had a decrease in duration following training, and Females- an increase.</p> <p>SKL-I vs. SKL-D: Effortful 10 mL: GENDER ($p = 0.006$, $d = 1.72$). Males had a decrease in duration following training, and Females- an increase.</p>
Peak 1-peak 2 duration	SKL vs. STR: Non-effortful saliva: GENDER*AGE ($p = 0.04$, $d = 0.81$) . Old/Females showed an increase ($p = 0.007$) in the relative duration

			following training, whereas young/males, Old/Males and Young/Females showed no change.
			SKL vs. STR: Effortful 10 mL: GENDER ($p = 0.07$, $d = 1.00$). Females had an increase in duration and Males had a decrease in relative duration following training
Onset1-Onset 3 duration			SKL vs. STR: Effortful saliva: TRAINING*AGE ($p = 0.047$, $d = 0.62$). Old in STR and Young in SKL had an increase (both non-significant) in duration following training, while in Young in STR training and Old in SKL had little change. SKL vs. STR: Effortful saliva: TRAINING*GENDER ($p = 0.015$, $d = 0.99$). Females in STR ($p = 0.049$) and Males in SKL ($p = 0.20$) had an increase in relative duration following training, while Males in STR and Females in SKL had little change.
Hyoid movement			SKL vs. STR: GENDER ($p = 0.049$, $d = 0.70$) Females had an increase in hyoid movement following training, whereas Males were had a decrease in hyoid movement ($p < 0.001$). Males in STR no significant effect ($p = 0.58$).
Submental muscle activity			SKL vs. STR: Effortful saliva: TRAINING ($p < 0.001$, $d = 1.11$) STR had a larger increase ($p < 0.001$) than SKL ($p = 0.65$) following training. SKL vs. STR: Effortful saliva: AGE ($p = 0.036$, $d = 0.65$). Young had a larger increase ($p = 0.01$) in peak amplitude following training than Old ($p = 0.03$). SKL vs. STR: Effortful 10 mL: TRAINING ($p = 0.004$, $d = 1.10$). STR had a larger increase ($p < 0.001$) than SKL ($p = 0.56$) following training. SKL vs. STR: Effortful 10 mL: AGE ($p = 0.07$, $d = 0.66$). SKL-I vs. SKL-D: Effortful 10 mL: TRAINING ($p = 0.064$, $d = 0.95$) SKL-I vs. SKL-D: non-effortful saliva: AGE ($p = 0.075$, $d = 0.97$) SKL vs. STR: non-effortful 10 mL: AGE ($p = 0.08$, $d = 0.65$) SKL-I vs. SKL-D: non-effortful water: AGE ($p = 0.03$, $d = 1.23$). Young had a larger increase in peak amplitude following training than Old.
CSA			NA
Performance during training	Hit rate		SKL-I vs. SKL-D: TIME ($p = 0.01$, $d = 1.45$). Both training groups increased hit rate during training.
	sEMG peak amplitude		STR: TIME ($p < 0.001$). The average of sEMG for each session increased over the course of training. STR: AGE ($p = 0.002$). Young had greater sEMG peak amplitude than Old, overall. STR: TIME*AGE ($p = 0.003$). Young subjects showed a greater increase in sEMG peak amplitude during the training sessions in comparison to Old.
Questionnaire			NA

CHAPTER 7: DISCUSSION

7.1 Introduction

A novel skill training approach emphasizing precision during swallowing with various degrees of effort (20-70% of maximal effortful swallow) was compared to a traditional training approach for swallowing rehabilitation that consisted of effortful swallowing. The concept behind this comparison was motivated from the motor learning literature. The development of skill training answers a need for an alternative approach to strength training in dysphagia rehabilitation for two reasons. First, muscle weakness is not always the pathophysiological basis for dysphagia, and since treatment should be prescribed based on pathophysiology rather than symptom, effortful swallowing might not be appropriate in certain conditions. Second, effortful swallowing has been reported to have negative effects that were both immediate (Bulow et al., 2002; Hind et al., 2001) and cumulative (Garcia et al., 2004).

This study serves as Phase I clinical-trial and, as recommended in the literature (Robey, 2004a; Robey & Schultz, 1998; Whyte et al., 2009), included several aims consistent with this level of research. The “activity” or changes occurring following skill training were assessed in comparison to that of effortful swallowing in healthy subjects (Robey & Schultz, 1998). Estimation of training effect sizes was accomplished using Cohen’s *d*. In addition, potential adverse effects were noted. Assessments of change at multiple levels using several outcome measures were conducted in order to identify the most sensitive outcomes. Finally, the a-priori alpha level was liberal and both significant ($\alpha \leq 0.05$) and marginally significant ($0.05 < \alpha \leq 0.10$) results were reported. Rather than correcting for multiple comparisons, caution was taken with interpretation of results in order to avoid Type I error, by identifying and interpreting *patterns* of change.

The skill training group was subdivided into two groups: skill training with immediate visual feedback and skill training with delayed visual feedback, with 10 subjects in each group counterbalanced for age and gender. This was done to explore potential differences in outcome measures due to the timing of visual feedback, based on reports from the motor learning literature, which imply superior performance for healthy subjects using delayed feedback during motor training (Swinnen et al., 1990).

Forty subjects were included in the study, equally representing two age groups and both genders. This allowed for assessment of age and gender effects on the changes following training. Age and

gender were not expected to affect the training results, but statistical analyses revealed significant interactions of both age and gender with training type. Thus, age and gender were included in the statistical models as factors.

The two training protocols (skill and strength training) consisted of high frequency training that included overall 1000 repetitions of swallowing (100 repetitions a day, 5 days a week, for 2 weeks), utilizing custom-made software (BiSSkiT) that provided guided training with biofeedback from the submental muscle group. Skill training aimed to increase precision of both time and force during swallowing, while effortful swallowing, which was chosen as the reference training, aimed to increase strength in swallowing. This single difference between the two training protocols allowed identification of differences between increased precision and increased strength.

Swallowing strength training was hypothesized to affect neurophysiological, biomechanical, and structural levels. The hypothesis was that muscle strength would increase as a result of an increase in neural downflow due to ‘strength learning’ of effortful swallowing execution. Increased downflow would presumably reflect more efficient and synergetic control of agonist and antagonist muscles (Kidgell, Stokes, & Pearce, 2011). However, a generalized contraction rather than submental-specific influence was expected since effortful swallowing has been reported to increase pharyngeal pressure (Witte et al., 2008) and decrease hyoid excursion (Bülow et al., 1999; Hind et al., 2001) suggesting that non-specific were produced. It was assumed that this generalized effect would be manifested as increased pharyngeal pressure and duration, decreased UES opening, decreased hyoid displacement, increased submental activation during effortful swallowing, and an increase in the submental CSA, relative to skill training. These changes would reflect an overall strengthening of the pharyngeal and hyoid-related muscles. Effortful swallowing has been suggested in prior research to have the potential for adverse effects on swallowing (Bülow et al., 1999, 2001; Garcia et al., 2004), and quantifying these effects was considered important as it is a frequently used approach. Swallowing skill training was hypothesized to affect neurophysiological and biomechanical substrates. The assumption was that increased neural downflow would occur as a result of this type of training. This would be manifested as swallowing-related increase in precision, including increased pharyngeal pressure and duration, decreased UES pressure, and increased submental activity in non-effortful tasks, relative to strength training. Increased pharyngeal pressure, reduced UES pressure, and increased submental activity during non-effortful swallowing would represent an improved efficiency in a functional swallowing task, and are important for pharyngeal clearance and reduction of aspiration in persons with dysphagia. These changes would indirectly reflect creation of new neuronal groups

that would enable the precise execution of non-effortful (i.e., functional) swallowing, indicating ‘skill learning’.

Over all, there were no differences between skill and strength training, other than increased sEMG activity in effortful swallowing task following strength training but not skill training. It is important to clarify that although only one difference was found, the difference between the approaches or the effect of a single approach versus a sham condition should still be explored in subjects with dysphagia. Differences between the two approaches in changes in activity are discussed in the next sections for each of the outcome measures.

7.2 Neurophysiologic changes

The current study included assessment of MEP magnitude as an outcome measure for comparing differences in M1 excitability following swallowing skill training in comparison to swallowing strength training. Few studies have used MEPs in healthy subjects as an outcome measure to document cumulative effects of swallowing training (Gallas et al., 2009; Macrae, 2011) or swallowing-related training (Svensson et al., 2003). Macrae (2011) did not find significant changes in MEP magnitude following either an effortful swallowing training protocol or a modified head-lift protocol employed in her study. Gallas et al. (2009) found an increase in MEP magnitude following one week of training of effortful swallowing of water. Svensson et al. (2003) found an increase in MEP magnitude at high magnetic stimulation levels and an expansion of tongue-related M1 area following a week of tongue protrusion training. Thus, M1 might have the capacity to accommodate, at least partly, the acquisitions of new motor tasks. Hence, neural adaptations of M1 were expected in the current study.

7.2.1 Changes in corticobulbar excitability following strength training

It was hypothesized that strength training would result in larger MEPs for submental contraction, in comparison to skill training when measured immediately after training (4.1.1 H1). Although statistical significance was not reached, a trend towards a difference between the training groups was apparent. The data indicated that swallowing strength training resulted in a trend towards an increase in MEP magnitude during submental contraction, relative to skill training. This trend was apparent when measurements were taken immediately after the last (10th) training session. It was also hypothesized that swallowing strength training would lead to greater submental contraction-MEP magnitude in comparison with skill training following the training period (Section 4.1.1 H4). Again, similar to the non-significant trend found in measurements taken immediately after

the 10th training, there was a trend towards a difference between the training groups in submental contraction-MEP measured 4 days after the training period ended. When testing the change within the strength group for statistical significance, there was a non-significant trend towards an increased magnitude. The effect sizes following strength training for the contraction task ranged from small after the first session to medium size after the last training session and post-training. For the saliva swallowing task, the effects ranged from zero to small.

As described by Folland & Williams (2007), following strength training there is an initial increase in voluntary neural drive that accounts for an increase in strength, followed by a later increase in muscle size. Indeed, the results of the current study documented a trend towards increased voluntary efferent neural downflow in submental contraction task. There are discrepancies in the evidence from the literature regarding the effects of strength training on MEP magnitude in muscles of the limbs, with some studies suggesting no changes (Jensen et al., 2005) and some support changes occurrence (Griffin & Cafarelli, 2007). Some studies support the occurrence of changes at the cortical level (Kidgell & Pearce, 2011; Rogasch, Dartnall, Cirillo, Nordstrom, & Semmler, 2009) and some suggest that changes occur at the spinal level (Adkins et al., 2006; Carroll et al., 2002) following strength training in muscles of the limbs.

The findings of Griffin & Cafarelli (2007) support the trend found in the current study towards increased MEP magnitude associated with voluntary contraction. They documented an increased MEP amplitude following 2 weeks of lower-limb (tibialis anterior) strength training in younger subjects (18-32 years). MEPs recorded during voluntary muscle contraction had a significantly higher magnitude at the 6th session and at the 12th (last) session compared with baseline, relative to a non-active control group. Rest-MEPs did not change following training. The maximal voluntary contraction torque increased significantly in the active group relative to the non-active groups. Griffin & Cafarelli explained the changes as neural adaptations, most likely at the cortical level, manifested as improved ability to repeatedly perform effortful muscle contraction, although they could not rule out effects on the spinal level.

The effects of swallowing strength training can be conceptualized as leading to creation of a motor plan for executing submental muscle contraction, due to the effects of 'strength learning'. This motor plan allows efficient generation of large forces (Burkhead et al., 2007; Griffin & Cafarelli, 2007). This could lead to high synchronization of motor-units firing patterns, recruitment of additional motor-units and increased firing frequency during submental contraction (Van Cutsem et al., 1998; Duchateau, Semmler, & Enoka, 2006; Leong, Kamen, Patten, & Burke, 1999; Milner-Brown, Stein, & Lee, 1975). The trend towards an increase in MEP magnitude immediately after the 10th strength training session and 4 days after the training period, in comparison to skill training, can indirectly support this speculation of increased efferent output.

Possibly, neurophysiological changes could have occurred to a larger extent in the other hemisphere that contained the 'non-dominant' hotspot. However, the method used in the current study in which MEPs magnitude was measured from one hemisphere only did not allow for their detection. Measuring MEP magnitudes from both hemispheres could be useful as swallowing is bilaterally innervated (Malandraki, Sutton, Perlman, Karampinos, & Conway, 2009; Martin et al., 2001). In addition, it is possible that M1 expanded following strength training. Utilizing M1 mapping for detecting potential submental-related M1 expansion could provide information regarding training outcomes.

In contrast to the findings of the current study, Carroll et al. (2002) found decreased MEP magnitude following resistance training of the index finger in younger subjects (22-36 years), although the maximal isometric strength of the muscles increased significantly. The authors proposed that since both TMS (that measures both I and D waves) and TES (that measures D-waves) demonstrated the same results of decreased magnitude, the decrease was related to reduced number of activated motor units and reduced firing rates of the motoneurons at the level of the spinal cord, without affecting the cortical function. Support to neural changes at the spinal cord level is also found in a study by Adkins et al. (2006). They reported an increased number of excitatory synapses in the spinal cord after strength training that involved repetitions of a new task with increased power but not after skill training that involved repetition of the same task but with less power. The current study utilized TMS only, without TES, and thus evaluation of specific changes in the corticobulbar track rather than changes at the corticocortical level could not be made. It is possible that these two levels were affected differently following swallowing training.

Jensen et al. (2005) compared skill training to strength training of the biceps. Strength training resulted in decreased rest-MEPs. A non-significant trend was found for reduced magnitude of contraction-MEPs. Jensen et al. suggested that the lack of novelty in the strength task, its simplicity, and the absence of visual feedback, made the strength task insufficiently challenging for inducing neural effects. The effortful swallowing protocol employed in the current study had a skill component as it required the execution of swallowing with visual biofeedback, with emphasis of the strength component during swallowing. Hence, it is possible that the trend towards neurophysiologic changes occurred in the current study following swallowing strength training due to the skill component.

7.2.2 Changes in corticobulbar excitability following skill training

Skill training was hypothesized to result in larger MEPs in non-effortful saliva swallowing task, in comparison to strength training, when measured immediately after training (4.1.1 H2) and when measured 4 days after the training period ended (4.1.1 H5). These hypotheses were not supported by the study. The effect size for the saliva swallowing task ranged from zero to small following skill training. However, for the contraction task, there was a medium effect size for measurements taken immediately after the 10th training session, with a trend towards decreased MEP magnitude at 90 min post training in comparison to baseline.

In contrast to the current study findings, reports in the literature provide support to the occurrence of neural adaptations following skill training. Two stages of cortical adaptations are usually described: early and late (Karni et al., 1995, 1998; Ungerleider, Doyon, & Karni, 2002). An increase in MEP magnitude was found early in the course of skill training, after 1 hour (Muellbacher et al., 2001), after 5 days (Pascual-Leone et al., 1995), and after 2 weeks of training (Jensen et al., 2005). These increases were later followed by a decrease in excitability. It is possible that in the present study changes did occur but were not captured since the evaluation was conducted at the beginning and ending of the training period. Muellbacher et al. (2001) found that following training of brisk pinching emphasizing fast and precise movement, there was a significant increase in M1 excitability after 60 min of practice. However, at follow-up (1-55 days post 1 hour of training), MEP magnitude returned to baseline value. One possibility is that 1 hour was not enough to encourage permanent brain plasticity, and the magnitude of MEPs returned to baseline. Another possibility is that 1 hour was indeed enough to allow plastic changes to occur and the increase in excitability after 1 hour of training reflected the occurrence of LTP/D processes, while the reduction in MEP magnitude at follow-up reflects a more efficient neural activation through reorganization (Donoghue, 1995; Ungerleider et al., 2002). Similarly, it is possible that no changes were identified in the current study since the time of assessments missed the transition from early to late changes. In another series of studies (Pascual-Leone et al., 1995; Pascual-Leone, Tarazona, & Catalá, 1999), 28 days of motor skill learning of a complex finger movement resulted in increased cortical representation of the hand muscle that was found as early as 5 days post training onset in younger subjects. Measurements taken up to 28 days into training revealed that the increase in M1 representation seen at 5 days into training was gradually reduced over the course of time. Jensen et al. (2005) found that 2 weeks of visiomotor skill training resulted in an increased magnitude of rest MEPs, an increased magnitude of contraction-MEPs, and decreased MEP threshold (the magnetic stimulation threshold required to elicit a minimal

response). The increase in excitability was maintained at 4 weeks into the training period, and reduced at 6 month post training to a level that was just above baseline but not different from it. Thus, following skill training in muscles of the limbs, different time frames of MEP changes were found. The expected time frames for changes in MEP magnitude following swallowing skill training have not been explored. This information could be useful for study design and can allow precise evaluation of neurophysiologic changes following training.

Another explanation for lack of neurophysiologic changes is that skill training was not challenging enough for healthy subjects since they usually swallow with precision. In order for adaptations to occur, the new motor task needs to be ‘novel’ in terms of neural circuits. Neural changes following skill training involve creation of new ‘specialized’ neuronal groups that allow efficient performance (Jensen et al., 2005; Karni et al., 1995; Ungerleider et al., 2002). Hence, a new skill must consist of a motor sequence that was not previously acquired. If the task consists of simply repeating a motor behaviour, that was already learnt, changes will not occur (Plautz et al., 2000). As documented in several studies by Svensson et al. (Boudreau et al., 2007; Svensson et al., 2003, 2006) the tongue protrusion task did lead to neural adaptations, perhaps due to task novelty. Alternatively, it is possible that members in the skill training group were not ‘pushed’ to achieve their maximal performance due to the training procedure. In strength training, the minimal threshold for the task was defined on a daily basis and was higher every day, thus demanding increasing levels of force. However, in skill training the target was always relatively large at the start of the session. Having a large target area allowed more room for imprecision. The target then gradually diminished in size. Perhaps having a target area that decreased its initial size every day would have increased the task complexity and might have consequently resulted in greater neural adaptations. Another possibility is that skill training was too challenging and a longer period was required for learning to occur. It is likely that skill training would provide enough challenge and novelty for persons with swallowing difficulties that require rehabilitation. It is also possible that skill training with delayed feedback led to neural adaptations, but due to the small sample size (10 in each subgroup), only large effects could have been detected. In addition, since younger subjects had increased submental activity in non-effortful tasks following skill training, but older subjects did not, it is plausible that younger subject had neural adaptations but these were not detected due to the sample size (10 young subjects in skill training).

Another consideration is that M1 might be more responsive and adaptable to voluntary tasks such as submental contraction, tongue protrusion (Svensson et al., 2003), skilled arm (Jensen et al., 2005), and skilled finger movements (Karni et al., 1995), than it is for swallowing. Possibly, the trend towards increased MEP magnitude following swallowing strength training was due to

changes in submental contraction, more than changes to pharyngeal swallowing. As discussed in Chapter 2, swallowing is controlled and mediated by the brainstem, with contribution from other brain areas including M1. Martin et al.'s (1997) study that located the areas in M1 that elicited swallowing following electrical stimulation, support the contribution of M1 to swallowing, although only a small number of these areas were found (Martin, Murray, Kemppainen, Masuda, & Sessle, 1997), supporting a limited contribution of M1 neurons to swallowing. However, Martin et al.'s study documented cortical control over reflexive swallowing rather than volitional, hence M1 contribution to volitional swallowing might be different and larger.

7.2.3 MEP differences between the first and the last training sessions

It was hypothesized that MEP magnitude recorded immediately after training would decrease from the first to the last (10th) training session during volitional swallowing tasks for skill training, and during the volitional contraction tasks for strength training (Section 4.1.1 H3). The results of the current study do not support this hypothesis, as no changes were documented when comparing MEP magnitudes after the first (at 5, 30, 60, and 90 min) and last (at 5, 30, 60, and 90 min) training sessions. The rationale for this hypothesis was that as motor training proceeded, some of the neural mechanisms that took place during the first stages of learning would be reduced due to consolidation of the learnt behaviour and neural reorganization (Rosenkranz et al., 2007).

Changes in MEP amplitude might have continued to take place later following an hour of intervention (e.g., up to 3 hours post-training). However, the current study design did not allow capturing of such changes. Hence, it is possible that measuring MEPs for a longer time period than 90 min after training, would have led to differences in MEP magnitude when comparing the first and last training sessions, and when comparing baseline measures to immediately post-training measures. Data from the current study indicated that at 90 min post training, an increase in MEP was still presents. Potentially, further increase in excitability might have occurred, but it was not captured in the current design. The choice of MEP measurements at up to 90 min after training was based on a study that documented the occurrence of LTP/D mechanisms up to two hours after their induction in vitro (Thompson et al., 2005), and on studies that documented maximal MEP changes at 60 min post swallowing-related intervention (Abdul Wahab et al., 2010; Doeltgen et al., 2010). It is possible that long behavioural training sessions, like the one used in the current study, could introduce different timing mechanisms. Measurements of swallowing-related MEP changes have been made in several studies that used a 60 min or 90 min time frame (Doeltgen et al., 2010; Fraser et al., 2002, 2003; Power et al., 2004). However, the intervention was shorter in most of these studies, for example, 5 min (Fraser et al., 2002), 10 min (Fraser et al.,

2002, 2003; Power et al., 2004), and 20 min of electric stimulation (Fraser et al., 2002). In these studies, MEPs magnitude was measured immediately after stimulation. In another study that included 1 hour of continuous electrical stimulation, MEPs were measured immediately after the session, and up to 90 min after it, but no changes were found (Doeltgen et al., 2010). It is possible that since the electrical stimulation used in the Doeltgen et al. study was not paired with swallowing, there were no changes in excitability. Other than the study by Doeltgen et al. (2010) and the current study that provided an hour-long intervention, no other studies in the area of swallowing investigated changes to MEP magnitude following 1 hour of intervention. Hence, perhaps using a longer time period in which MEPs are measures post-intervention is needed to document changes, and thus, the possibility of LTP/D occurrence can be captured. Alternatively, it is possible that there were no differences between the first and last training session, since no changes in excitability occurred following skill training or strength training. If any differences existed between the first and last training session for the submental contraction task, they might have been too small to detect.

7.2.4 Age effects on corticobulbar excitability

The influence of age was significant (after the 10th session for both tasks) and marginally significant (after the 1st session for both tasks) with older subjects having greater excitability than younger subjects overall. The influence of age was present at baseline measurements of excitability, and was further explored in Chapter 9. Briefly, older subjects had larger MEP magnitude in both tasks (volitional submental contraction and volitional saliva swallowing) than younger subjects. Since the effects of age were present at baseline and during the training period, with no interaction of age and time, it is can assumed that training did not change the MEP difference between the two age groups.

It is possible that older subjects in the current study had larger MEPs in comparison to younger subjects due to reduced inhibition, meaning that older subjects had increased excitation since the inhibitory input is reduced. Supporting this hypothesis is a study that utilized a paired-pulse procedure to measure intracortical inhibition, older subjects had decreased level of inhibition in comparison to younger subjects, when measuring limb muscles activation (Peinemann et al., 2001). This topic will be further discussed in Chapter 9.

7.2.5 MEP measurements: Methodological considerations and limitations

MEPs were not normalized in this study. Since MEPs were measured using sEMG electrodes, their magnitude might change from session to session depending on the location of the electrodes (De Luca, 1997). The proximity of the electrodes to the innervation points of the muscles by the motoneurons can influence the size of the muscle activity. In addition, recordings from different locations along the muscle (close to the tendon or close to the belly) can change the recorded response (De Luca, 1997). Thus, lack of normalization might have reduced the accuracy of the measurement when using a repeated measure design. Normalization of MEPs is often used in limb research by calculating a ratio between the size of the MEP to the size of the maximal response recorded by electrically stimulating the muscle itself, called the M-max (Keenan, Farina, Merletti, & Enoka, 2006; Kidgell & Pearce, 2010). The M-wave, also called the compound muscle action potential, can be recorded from the muscle by applying maximal electrical or magnetic stimulation over the peripheral nerve (Kamen & Gabriel, 2010). The applied stimulation activates Ia afferents which feed into the spinal cord and lead to generation of an action potential (Enoka, 2008). M-max (maximal M-wave amplitude) represents the maximal elicited electrical activity of the peripheral muscle, and requires activation of all motoneurons by providing a strong electrical stimulation. Normalization of MEPs by peripheral nerve stimulation and acquisition of M-waves has not been conducted in swallowing research. It is possible that since M-wave elicitation requires the presence of Golgi tendon organs, they cannot be used for swallowing-related muscles. Golgi tendon organs are not present in the lips, tongue, and jaw openers muscles including anterior belly of digastrics (Neilson, Andrews, Guitar, & Quinn, 1979). Jaw closing muscles, including the internal pterygoids, masseters, and temporalis do have Golgi organs (Neilson et al., 1979), thus, M-waves could be obtained from these muscles.

Another approach for normalization is to elicit an isometric maximal voluntary muscle contraction and use this level as the maximal value to which other measures are normalized (Burden, 2010; Norcross, Blackburn, & Goerger, 2010). Reports regarding use of this method of normalization in swallowing related muscles are sparse (Kashiwagi, Tanaka, Kawazoe, Furuichi, & Takada, 1995). Several papers point out that there are many variables and multiple approaches for normalizations of EMG data from limb muscles (Burden, 2010; Fischer et al., 2010; Norcross et al., 2010), each having advantages and disadvantages. This topic should be investigated in swallowing related muscles to clarify which approach can be used for normalization.

MEP data were collected only from the dominant hemisphere containing the submental hotspot. Hotspot identification was conducted once, during submental contraction execution at baseline.

Subsequent measurements were all taken from this location throughout the course of the study. A question could arise regarding this method of unilateral, rather than bilateral M1 assessment. The submental muscle group is composed of three pairs of muscles: anterior belly of digastric, mylohyoid, and geniohyoid (Jacob et al., 1989; Kahrilas et al., 1991). Reports from the literature suggest that for the mylohyoid muscles there is no difference in hemispheric dominance (Hamdy et al., 1996), while for anterior belly of digastric muscles there was a task related difference between rest and speech (Sowman et al., 2009) as expected from the long-known left-hemispheric dominance for speech tasks (McAdam & Whitaker, 1971). However, since swallowing was not utilized as a task in Sowman et al.'s (2009) study, it does not necessarily follow that left dominance of control applies to swallowing. There are no reports regarding hemispheric dominance over geniohyoid. The clear dominance difference for speech has not been found for swallowing, despite exploration through several fMRI studies (Martin et al., 2001; Mosier, Liu, et al., 1999). The literature suggests that hemispheric dominance for pharyngeal and oesophageal control varies among subjects and can be identified through MEP magnitude evaluation (Hamdy et al., 1996). Subjects in the current study had either a hotspot located in one hemisphere only, or when bilateral hotspots were identified, one side had a larger MEP magnitude relatively to the other side. There was a difference between the subjects in the submental hotspot hemispheric location, supporting the notion that dominance for submental neural control does exist, but it is idiosyncratic for each subject. The assumption was that changes in neural control would be manifested at the cortical area that sends the largest output to the submental muscles (i.e., hotspot). However, it is possible that if the area of the non-tested hemisphere (providing that the subject had recordable MEPs from both hemispheres) had been assessed as well, more changes would have been detected. Changes to the hotspot in the other hemisphere would have been of interest, since it is possible that training affected the neural control in both hemispheres, and, indeed fMRI studies have found bilateral activation of M1 during swallowing (Malandraki, Sutton, Perlman, & Karampinos, 2010; Martin et al., 2001). No other studies conducted bilateral assessment of cumulative effects of swallowing training. Cumulative effects of tongue protrusion training have been assessed bilaterally only by Arima et al. (2011) that measured changes in brain activation following an hour of training using fMRI. Scanning was performed at baseline, immediately after an hour of training, 1 day, and 7 days after the training. A significant increase in bilateral M1 activation was detected at 1 hour and 1 day after training.

In addition, it is possible that the training affected interhemispheric inhibition, but this was not measured in the current study. Changing the levels of inhibition might allow a more precise motor performance, as supported by a study that measured cortical excitability during discrete activation of the fingers and found that the intracortical inhibition is the mechanisms that allows this selective activation (Zoghi, Pearce, & Nordstrom, 2003).

M1 mapping procedures were also not employed in this study. Changes to M1 representation of the submental area might have occurred as supported by a study by Svensson et al. (2003) that explored unilateral changes in M1 mapping following 1 week of tongue protrusion training. Expansion of the M1 area that controls the muscles of the tongue was detected. M1 expansion would suggest that additional areas of M1 were activated during swallowing, indirectly reflecting reorganization processes by which horizontal afferents create neuronal activation groups that specialize in the execution of a skilled task.

M1 hotspot was found at baseline during submental contraction execution, which was assumed to represent the same hotspot for M1 control of submental activation during volitional swallowing. However, it is possible that these areas are spatially close but do not overlap. Hence, mapping M1 for volitional swallowing hotspot might have revealed a slightly different location, and would have potentially captured more changes in excitability. In addition, assessing pharyngeal and oesophageal MEPs might have revealed neurophysiological changes following swallowing skill training.

Assessing pharyngeal and oesophageal MEPs in addition to submental MEPs might have revealed neurophysiological adaptation following swallowing training. The changes detected in pharyngeal and oesophageal function following training, support this suggestion.

Single-pulse TMS technique was used in this study to assess corticobulbar projection from M1 to the submental muscles. It is possible that other neural changes occurred following training, but were not measured. For example, changes in control circuits between different areas of the brain. These would require employment of brain imaging techniques that document cortical function such as fMRI or brain connectivity such as diffusion tensor imaging (DTI).

As mentioned, another limitation is that MEP measurements were made from 5 min up to 90 min after training. It is possible that this period was too short to measure changes that might have occurred after 90 min.

Since only marginally significant trends, rather than significant results at the 5% level were found, a longer training period may have led to a greater difference in MEP magnitude between the training groups. The pilot study involving extended training aimed to give an estimate of this possible effect of increased dosage, however the small sample size was not sufficient for statistical testing for comparing the results between the two training group (see Section 7.8). Choosing a 2-week training period was based on studies that found changes in healthy subjects within this time frame in neurophysiological excitability (Jensen et al., 2005), neural reorganization (Svensson et al., 2003), and in functional improvement in persons with dysphagia

(Huckabee & Cannito, 1999). Moreover, Jensen et al. (2005) found that the greatest increase in excitability occurred within the first 2 weeks of limb muscle training and although changes in motor performance continued to occur at the third and fourth weeks of training, MEP excitability did not increase any further. It is possible that an extended training period using a larger sample size would have resulted in increased corticobulbar excitability in healthy subjects. However, it is also possible that 2 weeks of training are sufficient to induce neural adaptations in individuals with dysphagia, as indirectly supported by the results of Huckabee & Cannito (1999) that provided 1 week of intense training (10 sessions overall). Hence, one should consider whether indeed extending the training period in healthy subjects is a necessary step.

7.3 Pharyngeal and UES pressures

7.3.1 Pharyngeal and UES pressures: Differences between skill and strength training

7.3.1.1 Strength training

It was hypothesized that strength training, in comparison to skill training, would result in higher pharyngeal peak pressures and durations, higher UES pressure, and shorter UES opening in effortful swallowing. In addition, relative timing intervals between pressure events in the pharynx and UES would decrease, in comparison to skill training, in effortful swallowing (4.2.1 H6). There were no significant main effects of training type on pharyngeal and UES pressures, however there were significant interactions of training and gender or age.

Following strength training, males had significantly increased UES pressure in non-effortful 10 mL water swallowing. This finding of increased UES pressure was not documented in other studies investigating the immediate effects of effortful swallowing. The rationale in the current study was that the cumulative effects of effortful swallowing would have an overall strengthening effect. Hence, the pharyngeal muscles would strengthen and pull the hyoid posteriorly during swallowing, affecting UES opening. However, increased UES pressure was found only for males and only for one task, thus this finding might represent Type I error. In addition, as discussed in Section 7.5, males in strength training had no changes in hyoid movement following training. It is possible then that strength training had no effects on the UES opening in males.

Females demonstrated changes in opposite directions to the hypothesis. They had significantly decreased UES pressure in non-effortful saliva swallowing task, and a marginally significant decrease in non-effortful water swallowing tasks. This finding is supported by studies that found

decreased UES pressure when implementing effortful swallowing (Huckabee et al., 2005; Witte et al., 2008).

The interaction of training and age revealed that older subjects in strength training had a non-significant decrease in UES opening duration in effortful saliva swallowing task, and a non-significant increase in the relative time duration between onset of sensor 1 to the onset of sensor 3 in the same task, likely reflecting later UES opening. Interestingly, Hind et al. (2001) found a correlation between increased pyriform sinuses residue during effortful swallowing with increased age in healthy subjects. The current study supports her finding, as older subjects in strength training had a trend towards shorter UES opening. It is possible that when older subjects are swallowing with increased effort they decrease their precision or coordination. It is recognized that the number of older subjects in strength training is too small to draw strong conclusions, and only a trend was indicated by this interaction. However, future studies should investigate this point further using a larger sample size since strength training is usually prescribed to older subjects (e.g., after stroke).

Studies investigating the immediate effects of effortful swallowing in healthy subjects found contradicting results. Some found no differences in UES nadir between effortful and non-effortful swallowing (Bülow et al., 1999; Hind et al., 2001). Others found longer UES opening (Hind et al., 2001; Hiss & Huckabee, 2005) and lower UES nadir (Huckabee et al., 2005; Witte et al., 2008). These studies employ different age population, and gender was not taken into account as a factor. Possibly, controlling for gender and age might have revealed fewer discrepancies between studies. However, it is important to bear in mind that these studies investigated immediate, rather than cumulative, which might produce different results.

This study documented no cumulative effects of strength training on pharyngeal pressure. Again, studies investigating the immediate effects of effortful swallowing in healthy subjects found contradictive results. Some found increased pharyngeal pressure and duration at the upper pharynx and at mid-pharynx (Hiss & Huckabee, 2005; Huckabee et al., 2005; Witte et al., 2008). In contrast, Bulow et al. (1999) found no difference in pharyngeal pressure and duration at mid-pharynx when comparing between effortful and non-effortful swallowing tasks in healthy subjects. Cumulative effects of effortful swallowing in healthy were investigated by Macrae (2011) who also found no changes in pharyngeal pressures and UES function following effortful swallowing. Other than Macrae's study, no other study documented cumulative effects of effortful swallowing in healthy subjects.

Effect sizes for each group were provided to allow an estimate of possible changes following each of the trainings. This was done as part of the recommendations of Phase I in clinical research.

However, as this study did not include a control group, it is important to keep in mind that it is difficult to quantify and distinguish training-related effects from non-training order-related effects. In the effortful 10 mL water task, strength training had a large effect size on upper pharyngeal pressure duration ($d = 0.83$), and mid-pharyngeal pressure duration ($d = 0.67$), with longer duration following training. Since the confidence intervals do not include zero, this increase of 0.17 s in each sensor might represent a statistically significant increase. This data provides some support for the task specificity principle with influence on effortful swallowing tasks. Possibly these effects were not detected during the analyses since the differences in the changes between the groups were not big enough.

To summarize, there was no main effect of training type on pharyngeal and UES pressures. Strength training consisting on effortful swallowing was found to have specific positive effects on UES pressure in females during functional swallowing tasks. There was some indication for negative effects on the UES in older subjects, however this needs to be further investigated.

7.3.1.2 Skill training

Skill training was hypothesized to result in higher pharyngeal peak pressure and duration, lower UES pressure, and longer UES opening in non-effortful swallowing, in comparison to strength training (4.2.1 H7). As this is the first study to have investigated the effects of skill training on pharyngeal pressure events, the rationale was based on the assumption that increased precision infers improved pharyngeal contraction. The results of the current study do not support this hypothesis.

Male subjects in skill training had significantly decreased duration of UES opening in effortful 10 mL water swallowing tasks and a non-significant trend towards decreased UES opening duration in effortful saliva swallowing task. In addition, males had a marginally significant increase in UES pressure in non-effortful saliva swallowing task. Due to the low number of subjects in skill training subgroups, it was not possible to test for gender effects within skill training with immediate feedback and skill training with delayed feedback. Possibly, only one group or both groups had similar gender effects. This finding of decreased UES opening duration and increased UES pressure is supported by the finding of significant decreased hyoid movement in males following skill training. This pattern of changes indicate a possible negative effect of skill training on males and should be further investigating in future research using a larger sample size. Skill training might lead to restricted forward pull of the hyoid bone due to increase pharyngeal muscle strength creating a backward pull of the hyoid.

In addition, younger subjects receiving skill training had a non-significant trend towards decreased UES opening duration in effortful saliva swallowing task, a non-significant trend towards increased UES pressure, and a non-significant trend towards an increase in the relative time duration between the onset of sensor 1 to the onset of sensor 3, in the same task. Younger subjects in skill training also had a marginally significant trend towards increased submental activity following training in both non-effortful swallowing tasks (Section 7.4.3).

Skill training was designed to target precision, with the amplitude of the target ranging from 20-70% of the maximal submental activity during effortful swallowing. It is possible that younger subjects and males in skill training were actually working on muscle power in addition to precision, over-increasing the pharyngeal musculature strength.

There was a specific influence of skill training with delayed feedback on the peak amplitude at mid-pharynx. The skill training with delayed feedback group had decreased peak pressure at mid-pharynx in all tasks (effortful and non-effortful) following training in comparison the skill training with immediate feedback. Support to this specific effect of swallowing-related intervention on mid-pharyngeal pressure was found in Heck, et al.'s (2012) study of the effects of electrical stimulation of the submental group on pharyngeal pressure. A decrease in mid-pharyngeal peak pressure relative to baseline (pre-stimulation) measurements in non-effortful saliva swallowing was found. These changes were not present for effortful saliva swallowing, or for the upper pharynx (Heck et al., 2012). In the current study, the reduction in mid-pharyngeal pressure was detected in effortful and non-effortful tasks. Inspection of the other outcome measures (e.g., hyoid movement and submental activation) did not identify a possible reason for this change. Utilizing manofluorography could clarify the reason for this decrease.

Again, effect sizes were calculated to allow an estimate of possible changes following skill training. In the non-effortful saliva swallowing task, skill training had a medium effect size when measuring the change in mid-pharyngeal duration ($d = 0.54$), and the time duration between peak of sensor 1 to peak of sensor 2 ($d = 0.41$), with an increase in duration after training. The confidence intervals for the increased duration do not include zero, hence this might be a statistically significant increase. In non-effortful tasks of saliva and 10 mL water swallowing, skill training had increases in upper pharyngeal peak pressure with small-medium effect sizes ($d = 0.38$ for saliva, $d = 0.47$ for water). The confidence intervals do not include zero hence the increase might have been statistically significant. Hence, there is support for possible positive influence of skill training on pharyngeal pressure in non-effortful swallowing tasks, supporting the task specificity principle. To confirm this, a larger sample with a control group should be employed in future studies.

7.3.1.3 *Summary: Training effects on pharyngeal and UES pressures*

To summarize, there were no significant differences between skill and strength training in pharyngeal pressure measurements. Strength training had specific positive effects on the UES in females. Older subjects in strength training had an indication of some possible negative effects on the UES, which should be further investigated.

There is indication that skill training might lead to negative effects on the UES in males. Younger subjects had demonstrated a trend towards shorter UES opening and increased UES pressure. Since two protocols were utilized in the skill training programme, it is possible that only one of them was causing the negative effects on the UES. A larger sample size would be needed to further explore the trends found. In addition, the effects of changes to skill training specification should be investigated. Specifically, the amplitude range of the target should be reconsidered. Skill training with delayed feedback resulted in decreased mid-pharyngeal pressure, but the reason is not clear.

The effect size found were small to medium when assessing the effects of each training approach. Nonetheless, medium effect sizes may well reach statistical significance with larger number of subjects but the question of whether these medium effect sizes are of clinical significance is raised (Bothe & Richardson, 2011). However, it is likely that a study that consists of individuals with dysphagia would demonstrate larger differences following training, with larger clinical significance.

7.3.2 *Upper pharyngeal pressure: The interaction of age-by-gender*

During non-effortful saliva swallowing, there was a difference in the changes displayed by older females and younger males who had a trend towards an increase in upper pharyngeal peak amplitude in comparison with younger females and older males, who had little change. During the same task, older females and younger males had an increase in the relative time duration between the peak activity of the upper pharynx (sensor 1) and the peak activity of mid-pharynx (sensor 2), in comparison to younger females and older males who had little change. The difference reached significance in older females but not in younger males. Possibly with a larger sample size, statistical significance would have been reached. An increase in the relative time duration might be due to earlier activation of the pressure events at the upper pharynx. Alternatively, activity at mid-pharynx might have been delayed, leading to a longer relative time duration.

It is possible that older females and younger males have a greater ability to change the pressure events at the upper pharynx following training. A similar pattern of age-by-gender interaction was found in a study that investigated the tongue's maximum isometric pressure, mean pressure during swallowing, and the ratio between maximal pressure to swallowing pressure (i.e., muscle reserve) in younger (20-39), middle-aged (40-59), and older (60-79) subjects (Youmans, Youmans, & Stierwalt, 2009). Interestingly, females in the middle-aged and older groups had higher tongue pressure during swallowing than males in these age groups. In addition, males produced a decrease in swallowing-related tongue pressure with age. Hence, middle-aged and older females and younger males had a higher swallowing-related pressure. The same trend also appeared in the ratio between the tongue's maximal isometric pressure and the swallowing pressure (high ratio indicates less muscle reserve). Middle-aged and older females had lower muscle reserve in comparison to younger females, and younger males had lower muscle reserve in comparison to middle-aged and older males (Youmans et al., 2009). These findings can serve as support for the current study's finding, since the age and gender interaction in the current study was found in sensor 1, which is located behind the tongue.

According to the principle of initial values, those with lower initial values of strength would benefit more from training (i.e., show greater increase in strength) than those with higher values (for example see Winters-Stone & Snow, 2003). Thus, older females and younger males have more 'room' or capacity for changes during training than younger females and older males and, hence, they had an increase in the pressure at the upper pharynx and a possible earlier onset of the pressure activity at the upper pharynx.

7.3.3 Pharyngeal manometry: Methodological considerations and limitations

In the current study, the catheter was 'blindly' placed, without concurrent VFFS to confirm location and detect movement during the assessment session. Instead, visual inspection of the waveforms was used to confirm the distal sensor location at the UES. Manometry, in comparison with manoflourography, has disadvantages, especially when a bolus is introduced, and, potentially when large amounts of secretions are swallowed. The intrabolus pressure can preclude the detection of catheter movement during swallowing as it elevates the pressure and alters the waveform by its presence. It can also mask and elevate the contract pressure within the UES (Brasseur & Dodds, 1991; Olsson, Nilsson, et al., 1995). The occurrence of intrabolus pressure can only be evaluated during VFFS, but this requires exposure to radiation, which is difficult to justify in healthy subjects. Also, since the larynx elevates during swallowing (Butler et al., 2009), the catheter can move and change location slightly or come out of the UES. However, as visual

examination of the waveforms was conducted during data collection, this limitation was controlled.

Pressure was measured at two locations along the pharynx and at the level of the UES using unidirectional electrodes. Measuring changes in pharyngeal pressure using high resolution manometry which consists of circumference sensors placed 2.5 mm apart along the catheter could also be used to identify changes. Its application in research has been in identifying the immediate effects of some manipulation such as bolus size changes (Hoffman, Ciucci, Mielens, Jiang, & McCulloch, 2010) and swallowing manoeuvres including effortful swallowing (Hoffman et al., 2012). Its application in measuring cumulative changes has not been tested.

7.4 Submental muscle activity

7.4.1 Changes in submental muscle activity following strength training

Strength training was hypothesized to result in a greater increase in sEMG peak amplitude in effortful tasks but not in non-effortful swallowing tasks, in comparison with skill training (Section 4.2.2 H8). This study support this hypothesis. Possibly, the increase in peak amplitude indirectly reflects an increase in the firing synchronization of the motor units (Arabadzhev, Dimitrov, Dimitrova, & Dimitrov, 2010; Milner-Brown & Stein, 1975; Milner-Brown et al., 1975; Yao, Fuglevand, & Enoka, 2000). This hypothesis regarding increased firing synchrony with increased strength is supported by a study that compared the synchronization level of first dorsal interosseous (index finger) motor units between weightlifters, untrained individuals, and highly skilled musicians. The greatest degree of synchronization was found in weightlifters, and the least degree of synchronization was found in the musicians (Semmler & Nordstrom, 1998).

Surface EMG was used in the current study to quantify changes in submental activity. Other studies that evaluated the effects of strength training in limb muscles also utilized sEMG as an indirect measure of synchronization (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002; Van Cutsem et al., 1998; Milner-Brown et al., 1975; Moritani & DeVries, 1979; Yao et al., 2000). Increased sEMG amplitude was found to be influenced by increased synchronization of the firing motor units following strength training (Arabadzhev et al., 2010; Van Cutsem et al., 1998; Folland & Williams, 2007).

The current study found increased activity during effortful swallowing, which was the practised task, but not during non-effortful swallowing. This finding follows on the principle of task

specificity (Barnett et al., 1973). Support for this finding is found in a study that compared motor unit firing frequency between weightlifters and age-matched controls. Weightlifters had higher motor unit firing frequency measured by intramuscular EMG during maximal (100%) contraction, but not during 50% of maximal contraction (Leong et al., 1999).

7.4.2 Changes in submental muscle activity following skill training

Skill training, in comparison to strength training, was hypothesized to result in increased sEMG peak amplitude during non-effortful swallowing (4.2.2 H9). Changes were hypothesized to occur in non-effortful swallowing tasks since it is similar to the training task itself, due to the principle of task specificity. This hypothesis is partly supported by the findings. No differences in sEMG peak amplitude were found between the training groups in non-effortful tasks, however when examining the effects of training on younger and older subjects, younger subjects had a marginally significant increase in non-effortful tasks and older subjects had a significant decrease in non-effortful 10 mL water swallowing tasks. These findings support the principle of task specificity since changes occurred in the non-effortful tasks, but not in effortful swallowing tasks. This implies that skill training has a specific effect on submental activity in functional tasks. These changes were not detected when testing for differences between strength and skill training in non-effortful tasks probably since the current sample size allowed detection of large differences.

Older subjects had a significant but small decrease in sEMG amplitude in non-effortful water swallowing task, but no changes were identified in non-effortful saliva swallowing. As discussed in Section 7.4.1, sEMG can indirectly measure changes in synchronization, with high synchronization levels leading to increased sEMG amplitude. However, it is possible that small changes to synchronization cannot be detected by sEMG. In a study by Yao et al. (2000), a computerized model was utilized to simulate the effects of different levels of motor unit synchronization on sEMG amplitude and muscle force. Moderate and higher levels of synchronization were found to increase the sEMG output by 65% and 130%, respectively, without affecting the average muscle force. In a study by Keenan et al. (2006), the number of activated motor units was directly correlated to the sEMG amplitude only when the motor units that were participating in the activity were of random size (small and large). When the activation was only of small motor unit, only large motor units, or of only motor units that were close to the bipolar electrode, the correlation was modest (Keenan et al., 2006). Indeed, older individuals have changes in motor unit composition, with a loss of the larger motor units (Faulkner, Larkin, Claflin, & Brooks, 2007; Johnson & Duberley, 1998). These changes might affect the ability of

sEMG to detect small changes following training, as older subjects have less variability in the motor unit sizes. According to Yao et al.'s (2000) model and Keenan et al.'s (2006) study, sEMG can be used as a proxy measure for identifying changes in synchronization or changes in the number of activated motor units, with some limitations. It is possible that skill training resulted in decreased sEMG peak amplitude in older subjects due to age-related changes in motor units properties. Alternatively, intramuscular EMG could identify more changes following training in older subjects, thus utilizing it should be considered (Ling, Conwit, Ferrucci, & Metter, 2009), as discussed in Section 7.4.4.

7.4.3 Submental activity: Age effects

Results from the current study suggest that younger subjects had both an absolute and a relative larger increase in sEMG peak amplitude in comparison to older subjects in most swallowing tasks. It is possible that age-related hypotrophy in limb muscles due to loss of motor units (Berger & Doherty, 2010), which manifests itself as decreased degree of muscle activation (Kamen, 2005), can also explain age-related differences in the changes of submental activation following swallowing training. There are contradictory reports in the literature regarding the influence of strength training on younger versus older subjects. Some suggest similar relative changes and some suggest decreased change for older subjects than for younger subjects. For example, a study that compared the results of strength training of the leg muscles between younger and older subjects found that the relative change in force between age groups was similar, but the absolute change was greater for younger (Häkkinen et al., 1998). In contrast, another study found that younger subjects, in comparison to older subjects, had greater absolute and relative increases in the maximal contraction force following 9 weeks of strength training of the knee muscles (Lemmer et al., 2000). Another study documented changes in motor unit discharge rates following strength training in young and old subjects. Following the first week of training, the younger subjects had a greater motor unit discharge rate than older subjects at high levels of muscle contraction. However, following 6 weeks of training, older subjects had a large increase in firing rates, and at post 6 weeks training, there were no differences in firing rates between younger and older subjects (Kamen & Knight, 2004).

A recent study (Raue et al., 2012) found a difference between older and younger subjects in reaction to resistance training at the genetic level. Increase in muscle size and strength were correlated with adaptations in 661 genes, affecting mainly fast-twitching muscle fibres. Following training of the thigh muscle, younger subjects had more response at the gene level than older subjects. Raue et al.'s study supports the findings of the current study, with younger subjects demonstrating more changes than older subjects following training.

Lastly, it is possible that since measurements were taken 4 days after the last training session, the older subjects had insufficient time for muscle recovery following training. This is supported by a study that demonstrated that even at 96 hours (4 days) after one training session, older subjects had not fully recovered and the number of contraction repetitions were still lower than their baseline performance (McLester et al., 2003). Hence, it is possible that if the post-training assessment had been conducted, for example, a week later, the older subjects may have had more time to recover and their muscle activity would have been higher.

7.4.4 Submental sEMG: Methodological considerations and limitations

sEMG has been referred to in the dysphagia literature as a tool for assessing muscle activity (Huckabee & Steele, 2006; Lenius et al., 2009; Wheeler-Hegland et al., 2008; Yoshida et al., 2007). Crary et al. (2007) even refer to sEMG as a tool for describing swallowing physiology (Crary et al., 2007, p. 94). In other areas of research, sEMG is often referred to as a tool for assessment of efferent neural downflow, which is manifested by the level of synchronization, firing rates, and recruitment of additional motor units (Arabadzhiev et al., 2010; Folland & Williams, 2007). Although *muscle activity*, which is the term used in swallowing research, is obviously affected by neural downflow, sEMG is not directly referred to as a tool to proximately measure efferent neural activation.

Some studies utilized intramuscular EMG as direct measure of firing rates, synchronization, and additional recruitment of motor units, which are factors that are influenced by increased efferent downflow (Duchateau et al., 2006; Gabriel, Kamen, & Frost, 2006; Patten, Kamen, & Rowland, 2001; Semmler, Sale, Meyer, & Nordstrom, 2004). Surface EMG might not be a precise measurement tool for detecting small and medium changes in motor unit properties since it is influenced by other factors. For example, the size of the motor units, the intracellular action potential shape, muscle fatigue, the proximity of the motor units to the recording electrode, the conduction velocity of the axon and muscle fibres, and the thickness of the subcutaneous tissue underneath the electrode can all affect the signal (Arabadzhiev et al., 2010; Duchêne & Goubel, 1993; Farina, Merletti, & Enoka, 2004; Keenan et al., 2006). sEMG peak amplitude reflects an increase in neural drive but it can also reflect changes in the duration of intracellular action potential, which increases in fatigue and results in increase sEMG amplitude as well (Arabadzhiev, Dimitrov, Chakarov, Dimitrov, & Dimitrova, 2008). Hence, the sEMG amplitude has some limitations in distinguishing between central factors of increase neural drive to peripheral factors like muscle fatigue (Arabadzhiev et al., 2010). Intramuscular EMG has an advantage over sEMG, but it also has a disadvantage of being an invasive assessment tool.

Surface EMG normalization to a reference value was not conducted in the current study and might have affected the results. Normalization of the sEMG data is important since as discussed in Section 7.2.5 sEMG can be influenced from extrinsic factors such as electrode placement along the muscle and proximity to the motor end-plates and intrinsic factors such as the distance between the electrode and the muscle that is influenced by the thickness of fatty tissue, the number of active motor units, and muscle fibre type composition and diameter (De Luce, 1997). Normalization to a reference value taken during each measurement session can allow calibrating the raw EMG data to the specific variables influencing the EMG signal in the specific time of examination and the specific electrode configuration. This is important in repeated measures design such as the one employed in the current study.

Lastly, activity amplitude was assessed by measuring the peak of the rectified sEMG waveform. Since the sEMG signal is influenced by the proximity of the recording electrode to the muscle innervation point, the peak amplitude might be highly susceptible to be affected from this factor that might introduce extreme EMG values. The rectified waveform can also be used to assess the area under the curve, thus quantifying the whole activity detected by the electrodes. Another approach for amplitude quantification can be by squaring the raw EMG data, smoothing it and then calculating the squared root of the mean values (Mathiassen, Winkel, & Hägg, 1995).

7.5 Hyoid displacement

It was hypothesized that strength training, as opposed to skill training, would lead to decreased hyoid displacement (Section 3.2.3 H10), based on findings of reduced anterior hyoid movement in healthy subjects during effortful swallowing implementation (Bülow et al., 1999; Hind et al., 2001). This hypothesis was not supported by the findings. It was found that following skill training, males had reduced hyoid displacement. This finding can explain the increase in UES pressure in non-effortful swallowing task in males following skill training and shorter UES opening in effortful 10 mL water swallowing task.

Hyoid displacement was measured during non-effortful swallowing, but not during effortful swallowing. It is possible that skill training affected hyoid displacement in effortful tasks as well, as evident by shorter UES opening in effortful 10 mL water swallowing task in males following skill training.

By integrating the results regarding training effects on UES opening in males and in young following skill training with the results of increased submental activity in non-effortful tasks in young following skill training, it is possible that younger males in skill caused this effect of

restricted hyoid displacement. However, a larger sample size of young males is needed to confirm this.

7.5.1 Hyoid displacement: Methodological considerations and limitations

Hyoid displacement was measured using ultrasonography, which is influenced by the depth of the structure being imaged. Since subjects have differences in the anatomy of the neck, these can affect image clarity. For example, it was more difficult to achieve a clear image from subjects with thicker fat layer under the chin, and this might have influenced the accuracy of the data. In addition, swallowing with the bite block placed in the oral cavity might have introduced different level of difficulties experienced by the subjects. Some might have swallowed with effort while others did not. Since submental sEMG was not recorded concurrently, this possibility stands. Possibly, some subjects might have swallowed with different levels of effort at pre-training in comparison to post-training since they got used to the bite block. Since no control group was employed, it is difficult to distinguish between order effects and training effects. Lastly, although the stabilization unit fixated the mouth and transducer, there could still have been movement of the head, which could have interfered with the measure.

Lastly, hyoid displacement is the result of an angular movement composed of anterior and superior hyoid movement, with the anterior movement contributing to UES opening and the superior movement contributing to pharyngeal shortening and compression. In the current study displacement was measured by calculating the distance between the hyoid and the mandible at maximal displacement and at rest. Thus, changes in hyoid displacement measured in males can be the result of changes in elevation, changes in anterior movement, or changes in both. However, using the current methodology, a distinction between those cannot be made.

7.6 Cross sectional area of anterior belly of digastric muscles

It was hypothesised that strength training, as opposed to skill training, would result in an increase of the CSA of the submental muscle area (Section 4.3.1 H11). This hypothesis was based on studies that found an increase in CSA in muscles of the limbs following strength training (Folland & Williams, 2007; McCall, Byrnes, Dickinson, Pattany, & Fleck, 1996b; Moritani & DeVries, 1979; Welle et al., 1996), and was also based on a study of strength training of the tongue

(Robbins et al., 2005) in healthy subjects. The findings of the current study do not support this hypothesis.

Lack of change found in the current study might be explained in terms of decreased ability of depicting submental structures using the ultrasound equipment utilized in this study. Indeed, measuring the CSA of the geniohyoid, which is a relatively deep submental muscle, was not possible due to insufficient resolution of the ultrasonography equipment (See *Chapter 5* for details). The borders of the muscles were insufficiently clear to distinguish muscle from surrounding tissue. Alternatively, changes in the CSA might not have taken place. Macrae (2011) also did not detect change in submental CSA following the effortful swallowing training protocol she employed.

It is also possible that although the muscle activity increased following 2 weeks of strength training, the CSA did not, since the time frame was too short to lead to structural changes. This is supported by a study that examined adaptation of the knee extensor following 2.5 and 5 weeks of strength training in healthy adults. Although significant changes occurred in muscles strength, muscles thickness did not change (Blazeovich, Gill, Deans, & Zhou, 2007). Another study found similar results of increased muscle strength in the absence of hypertrophy in the first 3-5 weeks of training, after which changes in muscle size were apparent (Moritani & DeVries, 1979). Similarly, the current study documented increase in muscle activity but no changes in the CSA. Robbins et al. (2005) found an increase in the CSA of the tongue in older healthy subjects following a longer period of training (8 weeks) in comparison to the current study. In addition, they used MRI to detect the changes. Macrae (2011) compared MRI and ultrasonography for the acquisition of images from the submental muscle group for CSA quantification. She found a high correlation between the two measures, supporting the use of ultrasonography for submental CSA assessment. If effects were indeed present but not detected in the current study, they might be of small size, and hence of small clinical importance. In addition, it is possible that the low ultrasonography equipment has insufficient resolution for detecting changes.

To summarize, the current study did not identify changes at the structural level following swallowing strength training. However, the results regarding increased submental activity and increased neural excitation in effortful tasks that involve the submental muscle group, support the notion of neural adaptations occurrence, which usually take place prior to muscle hypertrophy (Burkhead et al., 2007; Folland & Williams, 2007; Moritani, 1993).

7.6.1 CSA: Methodological considerations and limitations

The ultrasonography equipment used in the current study might have decreased the measurement accuracy due to low resolution at the level of the muscles of interest. In addition, since the muscles of the floor of mouth lie in proximity to each other, it is difficult to identify the boundaries of each muscle and knowledge about the expected shape of the structure, rather than the objective shape itself might guide the measurer when muscle the boundary was identified.

7.7 Motor performance during training

In order to assess whether the new training protocols utilized in this study were inducing the expected improvements in motor performance during the training period, the target hit-rate in skill training, and the submental muscle group activity in strength training were measured during every training session.

7.7.1 Motor performance during strength training

The hypothesis was that there would be an increase in submental sEMG peak amplitude over the course of strength training (4.4.1 H12). The results support this hypothesis. Hence, the training goal of increased submental muscle group activation has been accomplished. In addition, the older subjects had a lower sEMG amplitude during training and although they demonstrated an increase in amplitude over the course of training, this increase was smaller than the one demonstrated by the younger subjects. This finding is supported by reports of differences in motor performance during strength motor tasks between younger and older subjects. In one study, the differences were related to high variability in performance in older subjects at the beginning of the training period, with improvement and stabilized motor output as training continues (Enoka et al., 2003). In another study that utilized a visuomotor tracking task, older and younger subjects demonstrated similar improvements in tracking error, but there was an interaction of age and time with older subjects demonstrating less improvement in performance than the younger subjects (Cirillo, Todd, & Semmler, 2011). In addition, it is possible that older subjects in the current study required more time for muscle recovery than younger subjects. This is supported by a series of studies by McLester et al. (2003) that compared muscle recovery following one session of strength training in young and old subjects. Recovery was measured by counting the number of repetitions of the strength task at 24, 48, 72, and 96 hours after the session. Following 72 and 96 hours, older subjects still did not fully recover from training, compared with young subjects. Hence, it is possible that since swallowing strength training was performed every day, older subjects did not

perform as well as younger subjects because their muscles were still recovering from the previous day.

7.7.2 Motor performance during skill training

It was hypothesized that skill training with delayed feedback would have a smaller change in target hit rate than skill training with immediate feedback (4.4.2 H13). The rationale was that the delayed feedback protocol introduces a more difficult training that requires reliant on intrinsic proprioceptive feedback, rather than extrinsic visual feedback.

Subjects in the delayed feedback protocol had two training session with immediate feedback at the beginning of the training period in order to introduce them to the task. This was supported by a study that found that the ability to imagine movement improves if preceded by actual practice of the movement (Cunnington et al., 1996). The hit rate was calculated twice. When the difference in hit rate was calculated as the change between the third and the last training session, skill training with delayed feedback group had a larger (n.s.) increase in hit rate in comparison to skill training with immediate feedback group. When the difference in hit rate was calculated as the change between the first and the last training session, skill training with immediate feedback group had a larger (n.s.) increase in hit rate than skill training with delayed feedback group. Hence, both skill training subgroups had made the greatest improvement in motor performance of the task over the course of the first few training sessions.

Learning a new task is characterized by two stages: an early stage in which the greatest amount of improvement in performance is made (Floyer-Lea & Matthews, 2005), and a later slow-learning stage in which a smaller amount of improvement is observed over the course of weeks of training (Karni et al., 1995, 1998; Ungerleider et al., 2002). Hence, it is possible that both skill training subgroups would have had a further increase in hit rate had training continued.

Skill training with delayed feedback offered a more challenging training. Neurophysiologic adaptations were compared between skill-immediate and skill-delayed groups, with no significant differences. However, due to the small sample size and the large variance within the measure, only very large effects could have been detected. Possibly, a larger sample size would have revealed greater neurophysiological changes following skill training with delayed feedback.

To summarize, motor performance of the task improved over the course of training. The skill training protocol was designed to increase accuracy during swallowing and, indeed overall, subjects in both protocols improved their performance and increased their hit rate. The improvement in performance was most likely accompanied or supported by neural adaptations

(Donoghue, 1995; Ungerleider et al., 2002). It is important to clarify that an improvement in task performance does not necessarily translate into improvement in functional swallowing, as indicated by the biomechanical outcomes, since swallowing is influenced by dynamic sensory information, while the task itself involved only a limited range of proprioceptive sensory information.

7.7.3 Motor performance: Methodological considerations and limitations

Performance was quantified as hit rate during skill training. Another way to quantify performance during training could be by calculating the size of the smallest target achieved (in pixels, and in relation to the size of the screen) or the size of the target at the last trial. This measure can give additional information regarding improvement in precision, whereas calculating hit rate only does not give information regarding the advances in precision, as a high hit rate could also be achieved when hitting a relatively large target.

7.8 Pilot study – extended dosage

Ten subjects who took part in the 2-week protocol were willing to extend their participation in the study to a 4-week protocol. Hence, recruitment was not selective and every subject who agreed to take part was included and, thus, there was no control over the number of subjects in the group and the type of the training groups included. Seven subjects from skill training, and three from strength training volunteered.

The hypotheses were that the trends detected after 2 weeks of training would be further changed in the same direction. It is important to keep in mind that only very large effect sizes could have been detected given the small sample size of seven (and for some measures – six) subjects, hence inability to detect these differences at the level of 5% error probability does not mean that medium or large effect sizes were not present. For example, for a given power of 0.8, six subjects would allow detection of $d \geq 1.5$ effect size. Hence, the hypotheses for the 4-week protocol should be altered to identification of *very large* effect sizes. The results of the study marginally support the hypotheses.

The low number of subjects and their affiliation to different training groups prevented the use of parametric analysis. Instead, non-parametric analysis was conducted for the skill training group and descriptive statistics were used as well. Following 4 weeks of skill training, there were further changes in pressure durations at the pharynx and the UES, and a marginally significant difference

in target hit rate when comparing skill training with immediate feedback group to skill training with delayed feedback group. There were no significant effects of time when measuring hyoid movement, CSA of anterior belly of digastric, and submental muscle activity. MEP magnitude was not tested since the number of subjects with recordable MEPs was small ($n = 4$), and no apparent trends appeared when the data were examined visually.

Following 4 weeks of strength training, there were no apparent trends when visually examining the data. Again, with only three subjects, only very large effect size could have been detected statistically.

Skill training led to longer pressure duration at mid-pharynx during non-effortful water swallowing. This was in addition to a similar change detected in the 2-week protocol when examining the effects of age and gender among skill training in the same task. Since the members of the 4-week protocol were mostly from the older group ($n = 5$), it is possible that the effect was detected due to age effect. In addition, there was a marginally significant trend towards an increase in UES opening duration in non-effortful swallowing tasks. This effect was not found when analysing the 2-week training results. Hence, these findings support the hypothesis (4.2.1 H6) regarding an increase in duration in non-effortful tasks following skill training. However, the extended-dosage study did not explore differences between the immediate and delayed protocols due to the small sample size in this pilot study. Hence, it is possible that the changes found in the 2-week protocol of reduced pressure at mid-pharynx following skill training with delayed feedback, were still present following 4 weeks of training. Therefore, it is important to better understand what is the extent of the changes following 4 weeks of training for each of the skill training protocol. It is possible that each subgroup results masked the other group results, and the real effects following 4 weeks of training still need to be explored. Again, as no control group was employed and no between-group comparisons were made in the pilot study, it is difficult to quantify training effects from order effects that are not training-related.

In addition, skill training with delayed feedback group had a greater increase in hit rate ($p = 0.08$) than skill training with immediate feedback group when calculating the hit rate change from the 3rd to the 18th (last) training session. When examining the results of the 4-week versus the 2-week training, skill training with delayed feedback group continued to increase the hit rate (4.4% increase from the 3rd to 10th, and 7.0% from third to 18th training session), but skill training with immediate feedback group did not (1.4% increase from the 3rd to 10th, and 0.5% from 3rd to 18th training session). This finding indicates that during the additional eight sessions, learning continued to occur and motor performance during the task continued to improve in the skill training with delayed feedback protocol. This trend signifies that, as expected, skill training with delayed feedback provided a more challenging task than skill training with immediate feedback.

Providing a complex skill task during motor learning can encourage neural adaptations (Cirillo et al., 2011; Jensen et al., 2005; Nudo, 2006a). Based on these findings, it is possible that substantial neurophysiologic adaptations occurred in skill training with delayed feedback during the extended dosage protocol, however the small sample size did not allow for detecting them statistically.

7.9 Participants' subjective ratings of the swallowing training

It was hypothesized that skill training would exhibit more positive subjective ratings than strength training (4.5.1 H12). However, the results of this study did not identify significant differences at the 5% level, although a trend towards the skill training with delayed feedback group having higher positive ratings than the other two groups was indicated by the data.

Analysis of the subjective ratings assessed by a questionnaire completed by all subjects at the end of the training period did not identify significant differences between skill training and strength training in their level of enjoyment or dislike of the training task, nor in their rating of swallowing training outcomes like improvement in swallowing. Nonetheless, skill training with delayed feedback group demonstrated a trend towards rating their swallowing outcomes as more positive, and strength training group members rating their swallowing outcomes as more negative. In addition, and as mentioned before, seven subjects from skill training, but only three from strength training volunteered to participate in the 4-week training. This difference in itself might imply that subjects in strength training were not motivated enough to carry on for additional eight training sessions. Hence, although the differences in ratings were not significant, integrating the trend towards difference in ratings together with the low compliance for additional training in the strength training group, might indicate less enjoyment in the strength training protocol. The subjects who did continue into the 4-week training ($n = 10$), showed a trend towards higher ratings of positive questions and lower rating of negative questions than subjects in the 2 weeks protocol.

As stated by Logemann (2005) determining compliance and recording the complaints regarding the training programme is an important step in evaluating training outcomes in healthy subjects. It is possible that individuals with dysphagia will show different results in either direction (higher or lower satisfaction) due to the presence of a need to solve their swallowing problem. However, knowing how healthy subjects rated their training can assist in evaluating the possible strengths and weaknesses of each training protocol.

Since all training protocols in the 2-week training programme consisted of the same frequency and dosage, the trend towards different ratings was influenced by the characteristics of the protocols. Strength training seemed to be experienced as boring, and although biofeedback was provided to serve as a reinforcement tool, the repetitive task and lack of variability in training were perhaps not motivating enough. On the other hand, skill training with delayed feedback that was characterized by high variability and required attentiveness to the task seemed to be perceived as more beneficial to swallowing function. The delayed training protocol requires the trainee to pay close attention to the biofeedback signal. This might have given the subjects a feeling of involvement and responsibility on their score (hit rate), which they were introduced to at the end of the session. Interestingly, by subjective impression, subjects in the skill training protocol were quite interested in their score. In contrast, subjects in strength training were given their mean sEMG amplitude for the session, but fewer subjects were interested in the score, compared with skill training. Support for this trend was found in a recent study (Kothari, Svensson, Huo, Ghovanloo, & Baad-Hansen, 2012) that compared the ratings of three types of tasks: tongue protrusion against resistance of 1 N, against 3 N, and a complex tongue movement task. In the complex task, the subject had a magnetic disk on their tongue with which they played a computer game that required 2-dimensional movement, by using their tongue to control the cursor on the screen from a distance. Each task was performed for an hour following which the subjects were asked to rate fun, fatigue, pain, and motivation on a 0-10 scale. The complex task was rated with higher fun and motivation scores and less fatigue and pain, than the other two tasks. Another paper discussed the importance of motivation and high attention focus of the trainee on motor learning (McNevin, Wulf, & Carlson, 2000). Nonetheless, training ratings cannot be interpreted in isolation, and increased levels of enjoyment do not necessarily indicate beneficial results, as discussed in this chapter, with a possible adverse effect of skill training with delayed feedback on pharyngeal pressure.

7.10 Summary

The submental muscle group plays an important role in hyolaryngeal excursion (Pearson et al., 2012). Thus, targeting the submental muscle group during swallowing training is of importance, which has been recognized by several researchers (Shaker et al., 1997; Wheeler-Hegland et al., 2008). As suggested by Wheeler et al. (2008), targeting this muscle group during a training task that emphasizes high intensity and task specificity, might induce adaptations at the neural, biomechanical, and structural levels.

In the current study, submental sEMG biofeedback was utilized, using custom-made training software. Subjects in the strength training protocol were encouraged to gradually increase

strength, by working on 100% of the maximal submental activation during effortful swallowing, and increasing it by 10% after three successful effortful swallows (i.e., hitting the 100% threshold). Subjects in the skill training protocol were encouraged to increase their precision during swallowing by hitting a target area that was reduced in size by 10% after three successful hits and appeared at random times and random heights on the screen, ranging from 20-70% of the maximal submental activity.

Training was frequent (each day for 2 weeks and 4 weeks) and each training session comprised 100 repetitions over 1 hour. A recent review study found that individuals with stroke spend only 60% of the physiotherapy session time being physically active, although the treatment goal was to improve motor function. The authors stated that although the precise dosage for achieving optimal outcomes is still unknown, maximizing the activity time in therapy should be enhanced (Kaur, English, & Hillier, 2012). Hence, although not all outcome measures showed significant changes in the current study, there is still importance in investigating high-intensity training protocols in swallowing, based on a theoretical basis (Dobkin, 2005) and evidence from the literature (Bhogal, Teasell, & Speechley, 2003; Kwakkel, 2006; Kwakkel, Wagenaar, Twisk, Lankhorst, & Koetsier, 1999)

Although the name of the strength training programme introduced in the current study suggests an emphasis on increased muscle strength only, the task itself consisted of swallowing with effort. Thus, it included a skilled component as well as a strength component. The name ‘strength training’ was meant to create a distinction between the two training approaches: one emphasising skill in swallowing and the other emphasising strength in swallowing. Resistance training can enhance three elements of muscle performance: strength, power and endurance. Muscle power is the rate in which the force is being produced (Kisner & Colby, 2007). Since effortful swallowing requires fast execution of large forces, it can be categorized as power training. In addition, it is likely that endurance was also improved and was an important part of the training outcomes. This is supported by a study by de Lateur (1996) that found that the occurrence of muscle fatigue following motor exercise leads to recruitment of type I (slow twitching) and type II (fast twitching) motor units and therefore improves both muscle strength and endurance. Since the strength training protocol included 100 repetitions of swallowing with maximal contraction, with a 30-s gap between each swallow, it is possible that muscle fatigue occurred. However, this has not been assessed. Hence, it should be taken into account that the effortful swallowing protocol used in this study emphasized muscle power and endurance, as well as skill. If one imagines a conceptual spectrum for swallowing training ranging from *skill* on the one hand to *strength* on the other, the swallowing skill training offered in this study would be located close to the *skill* end,

whereas the strength training protocol utilized in the current study would be located closer to the middle of the spectrum.

Since the current study serves as phase I clinical-trial, the primary goals were to find an appropriate protocol for inducing adaptations, to estimate effect sizes, to identify adverse effects, and to identify the most sensitive outcome measures that indicate changes. The effect of each training approach was quantified using Cohen's *d*. The effect sizes found were small in MEP measures, anterior belly of digastric and hyoid movement, and the effect sizes in manometry pressure and duration measures were mostly small as well. The effect sizes were medium-large in submental activity measures for the strength training group. This information indicates that sEMG submental activity measurement could be used to measure changes following strength training. Large effect sizes were indicated in performance measurements. Hence, changes in performance occurred however with no measurable changes other than increased submental activity.

Potential negative effects were indicated when measuring hyoid movement and pharyngeal pressures. Thus, monitoring those for similar changes would be important in future studies. Following strength training, a trend towards shorter UES opening duration in older subjects was found, but this should be further investigated. Skill training with delayed feedback resulted in a decrease in the pressure at mid-pharynx. Males in skill training had reduced hyoid displacement, a trend towards increased UES pressure in non-effortful saliva swallowing and shorter UES opening duration in effortful tasks. In addition, younger subjects in skill training had a trend towards reduced UES function in effortful tasks, while no changes in submental activity were present in effortful tasks. Possibly, younger subjects in skill training and male subjects in skill training had increased pharyngeal strength, which restricted hyoid movement by pulling it posteriorly. The target amplitude was up to 70% of maximal submental contraction, which might be high in value in younger subjects, hence increased muscle power might have taken place.

In addition, the study aimed to find differences between the two approaches. The only significant difference between the two approaches was in submental activity, with strength training resulting in increased activity during effortful swallowing tasks in comparison to skill training. Strength training also resulted in a trend towards an increase in submental contraction-MEPs in comparison to skill training. Females had reduced UES pressure following strength training. Skill training resulted in no changes in M1 excitability in saliva swallowing task. There was a marginally significant increase in submental muscle group activity in non-effortful tasks in younger subject in comparison to strength training.

The trend towards increased neural drive for volitional effortful-type tasks (i.e., effortful saliva swallowing, effortful water swallowing, and submental muscle contraction) in strength training,

supports the task specificity principle of motor learning. The trend towards increased submental activity in non-effortful swallowing in younger subjects following skill training also supports this principle.

Skill training with delayed feedback resulted in greater changes during task learning, than skill training with immediate feedback, but overall skill training with immediate feedback had a higher hit rate than skill training with delayed feedback. Strength training was also characterized by increased submental sEMG amplitude during training.

Age and gender interacted with training type and influenced changes in pharyngeal pressure and changes in submental sEMG amplitude. These influences might be related to initial values of certain groups that allow more 'room' for adaptations.

The results of pilot study that examined the effects of an extended dosage of training were difficult to interoperate due to the small sample size, which allowed detection of only very large effects. However, there were significant and marginally significant effects of skill training on mid-pharyngeal and UES pressure duration events, with a marginally significant increase in target hit rate in the SKL-D group in comparison with SKL-I.

PART III: SKILL TRAINING IN DYSPHAGIA

CHAPTER 8: SWALLOWING SKILL TRAINING IN PATIENTS WITH DYSPHAGIA SECONDARY TO PARKINSON'S DISEASE

8.1 Introduction

This pilot study implemented swallowing skill training in individuals with dysphagia secondary to Parkinson's disease (PD). The aim was to document changes in submental sEMG peak amplitude and to measure motor performance during training.

There is support for the use of skill training approaches to the alleviation of motor symptoms associated with PD (Morris, Martin, & Schenkman, 2010; Platz, Brown, & Marsden, 1998; Rostami & Ashayeri, 2009). In addition, neural impairments in PD are manifested as reduced ability to plan motor acts based on internal cues (Cunnington, Iansek, Bradshaw, & Phillips, 1995; Cunnington, Iansek, Johnson, & Bradshaw, 1997). Thus, providing external cues can bypass the deficit neural mechanisms and improve function. The specific nature of this disease requires specific and targeted rehabilitation programmes. However, no specific rehabilitation approach is available for alleviating the symptoms in individuals with dysphagia secondary to PD, although the prevalence of dysphagia in PD is high (Kalf, de Swart, Bloem, & Munneke, 2012).

As mentioned in Chapter 1, data from this cohort of subjects was collected by a Master's student (Athukorala, 2012). The current chapter presents the results of submental muscle activity and motor performance during skill training, which were not presented in the Master's thesis, and were analysed by the researcher (O.S.).

8.2 Literature Review

Estimates of the prevalence of dysphagia in patients with PD range from 18% (Mutch et al., 1986) to 95% (Nagaya et al., 1998; Wintzen, Badrising, Roos, Vielvoye, Liauw, et al., 1994). This wide range can be a consequence of the method of investigation, where self-report of dysphagia tends

to fail in identifying dysphagia due to lack of awareness of swallowing difficulties in this population (Miller et al., 2009; Robbins, Logemann, & Kirshner, 1986). Instrumental evaluation can identify dysphagia more accurately and thus studies using this modality report higher dysphagia prevalence (Bird, Woodward, Gibson, Phyland, & Fonda, 1994; Felix, Corrêa, & Soares, 2008; Miller et al., 2009; Walker, Dunn, & Gray, 2011). Disease stage was found to correlate with dysphagia prevalence and it was estimated that up to 80% of all patients will have oropharyngeal dysphagia during the early stages of the disease (Coates & Bakheit, 1997), and in the advanced stages of the disease, the incidence of dysphagia can increase up to 95% (Nagaya et al., 1998; Wintzen, Badrising, Roos, Vielvoye, Liauw, et al., 1994). Disease severity was found to be correlated with swallowing difficulties in some studies (Coates & Bakheit, 1997) but not others (Ali et al., 1996; Rodrigues, Nóbrega, Sampaio, Argolo, & Melo, 2011; Walker et al., 2011). In addition, decreased gross motor function was associated with increased dysphagia (Walker et al., 2011).

Dysphagia symptoms in Parkinson's disease

Swallowing difficulties have been reported for all phases of swallowing: oral, oral transit, pharyngeal and oesophageal phases (Johnston et al., 1995; Leopold & Kagel, 1997; Nagaya et al., 1998). The motor symptoms of bradykinesia (slowness of movement), muscle rigidity, and prolonged initiation and reaction time demonstrated in limb muscles (Bloxham, Mindel, & Frith, 1984; Evarts, Teräväinen, & Calne, 1981) are also demonstrated in the oropharyngeal muscles (Bushmann, Dobmeyer, Leeker, & Perlmutter, 1989; Volonte, Porta, & Comi, 2002).

Dysphagia symptoms reported in the literature include slowness and prolonged duration of swallowing, prolonged premotor time (Nagaya, Kachi, & Yamada, 2000; Segura et al., 1995), prolonged oral phase processing due to abnormal lingual control, and piecemeal deglutition (Bird et al., 1994; Robbins et al., 1986). All of these can indicate reduced oral phase efficiency. In addition, presence of drooling in 78% of PD was reported, which might be explained by poor labial and lingual function (Johnston et al., 1995). Longer oral transit duration (Volonte et al., 2002), delayed pharyngeal swallow (Bird et al., 1994; Robbins et al., 1986) and aspiration in 25-50% of PD (Bird et al., 1994; Johnston et al., 1995; Robbins et al., 1986) can indicate mistiming of the motor event that might lead to aspiration. Vallecula and pyriform sinuses residue (Bird et al., 1994; Robbins et al., 1986) indicate difficulties in pharyngeal clearance either due to reduced pressure, or mistiming. These can lead to post swallowing aspiration/penetration if not cleared. Indeed, decreased sensitivity in the mid- and hypo-pharynx to tactile stimulation was found in this population and might be the underlying cause for aspiration (Rodrigues et al., 2011). Dysphagia in PD decreases the efficiency of feeding and drinking, and thus can lead to dehydration and weight loss (Johnston et al., 1995; Lorefält et al., 2004). In addition, dysphagia in PD can cause

social challenges and impact family members (Manor, Balas, Giladi, Mootanah, & Cohen, 2009; Miller, Noble, Jones, & Burn, 2006).

Swallowing treatment in individuals with Parkinson's disease

Despite the high prevalence of dysphagia in PD, few studies have documented the effects of swallowing training in individuals with PD (Baijens & Speyer, 2009; Russell, Ciucci, Connor, & Schallert, 2010). Nagaya et al. (2000) documented a significant reduction in pre-motor time, indicating improvement in swallowing efficiency, after a 20-min long training session that included oral motor exercises and Mendelsohn manoeuvre; however, this study did not investigate carryover into functional swallowing outcomes. Heijnen, Speyer, Baijens, & Bogaardt (2011) compared three treatment procedures in PD subjects with dysphagia, including (1) traditional dysphagia treatment, (2) traditional dysphagia treatment combined with NMES at a sensory, and (3) traditional dysphagia treatment combined with NMES at a motor level of stimulation. Treatment included 13-15 sessions, 30 min each, 5 days a week, for 3-5 weeks. All groups demonstrated similar improvement in Dysphagia Severity Scale and swallowing-related quality-of-life questionnaire (SWAL-QOL). There was no evidence in favour of any of the three treatment options.

Positive influence on swallowing was reported after respiration training and voice therapy. Expiratory muscle strength training (EMST) which involves blowing air into a mouth piece against resistance, has been documented to improve cough function and decrease penetration and aspiration (Pitts et al., 2009). In a randomized sham-controlled trial in a group of 60 individuals with dysphagia secondary to PD, EMST exercise was compared to a sham exercise. There were significant differences in outcomes between the EMST and sham exercises, with decreased aspiration and penetration and increased hyoid displacement during UES-related events. These events likely indicate that the strength training of the submental muscles which is achieved using the EMST exercise can increase the anterior-superior pull over the hyoid bone during swallowing, leading to improved pharyngeal clearance (Troche et al., 2010).

Lee Silverman Voice Therapy (LSVT) is a voice therapy technique designed specifically for individuals with a voice disorder secondary to PD (Ramig et al., 2001). Following intensive voice therapy, an improvement was documented in the functional level with increased voice intensity, and in the neuro-muscular level with improved oral and pharyngeal tongue function. A carryover effect on swallowing was present due to a generalized influence of training on the oral mechanism, and was manifested as improvement in oral-phase dysphagia (El Sharkawi et al., 2002). However, it is important to emphasize that in clinical practice, LSVT would be prescribed

for patients with voice disorder, rather than serving as the primary therapy for patients with dysphagia.

Despite swallowing difficulties in PD patients having distinct characteristics, no training approach has been specifically tailored and validated to address this problem. Designing dysphagia rehabilitation programmes that address relevant swallowing difficulties in PD has the potential to alleviate dysphagia symptoms. It is important to emphasize that swallowing rehabilitation in this population is limited by the nature of the pathophysiology in PD. The BG and other neurological structures that are impaired in PD are, at this stage, not curable. Hence, although dysphagia can be alleviated or compensated for, true recovery is not feasible.

The importance of external cues in Parkinson's disease

In healthy subjects, the SMA is involved in planning and temporally organizing sequential movements that are internally and externally cued (Cunnington et al., 1995). This activity precedes, and is completed prior to, the motor act (Cunnington et al., 1997; Schell & Strick, 1984). During the preparatory stage of an internally cued motor act, the BG sends neural signals to the thalamus that consequently sends signals to the SMA (Cunnington et al., 1997; Schell & Strick, 1984). In PD, impairments in BG function adversely influence SMA activation during internally-cued movements (Cunnington et al., 1995, 1997). Unlike healthy subjects, people with PD have delayed and longer SMA activation during internally cued motor acts (Cunnington et al., 1995, 1997). In contrast, externally-cued movements largely bypass the BG since the external cues reduce the need for BG involvement in motor planning (Cunnington et al., 1995). Thus, it is therefore possible that people with dysphagia secondary to PD might specifically benefit from swallowing training that provides external cues for the execution of swallowing.

Providing external cues by utilizing visual biofeedback can be beneficial for promoting motor learning. However, the frequency at which feedback is provided is also an important consideration. Guadagnoli et al. (2002) compared the performance of a simple motor task involving hand movement in a certain direction, between two groups of patients with PD. One group received 20% feedback (i.e., every fifth trial) and the other – 100% feedback. The errors during acquisition and during retention tests were compared between the groups. PD patients in the 100% feedback group had fewer errors during acquisition and during retention, than the PD patients in the 20% feedback protocol. These results were compared in the same study to healthy controls that demonstrated the opposite trend. Healthy controls in the low frequency (20%) feedback group had fewer errors during retention than healthy controls in the high frequency (100%) feedback group. The results of the healthy group are supported by the literature. High frequency feedback can impair the internalization of the sensory feedback associated with the task

performance, and can lead to over-reliance on external feedback (Rose & Robert, 2006; Salmoni et al., 1984; Schmidt & Lee, 1999). Since individuals with PD have an impaired ability to integrate sensory and motor information, they are reliant on external feedback, as proposed by Guadagnoli et al. (2002). Thus, there is support for using external cues to increase control over motor performance and for using frequent feedback to learn a new motor task to prompt learning in individuals with PD (Georgiou et al., 1993). External and frequent cues for motor function should lead to bypassing the impaired BG and allow the SMA to better contribute to motor planning, resulting in improved motor control.

Muscle strength in Parkinson's disease

Individuals with PD have reduced muscle strength of the limbs than healthy controls (Allen, Canning, Sherrington, & Fung, 2009; Allen, Sherrington, Canning, & Fung, 2010; Cano-de-la-Cuerda, Pérez-de-Heredia, Miangolarra-Page, Muñoz-Hellín, & Fernández-de-Las-Peñas, 2010; Stevens-Lapsley, Kluger, & Schenkman, 2012). The reason for this weakness is not known but may be a primary or a secondary symptom due to aging or disuse (Cano-de-la-Cuerda et al., 2010; Morris et al., 2010). Weakness has been identified in skeletal muscles and was associated with decreased mobility skills, gait speed, and falls in older individuals (Chandler, Duncan, Kochersberger, & Studenski, 1998) and in PD (Falvo, Schilling, & Earhart, 2008). It is also possible that individuals with dysphagia secondary to PD have weakness in the muscles that participate in swallowing. The strength of the submental swallowing muscles have not been compared to those of healthy controls. On the basis that weakness is present, it is possible that swallowing treatment that targets a functional or skilled component would also increase muscle strength, or vice versa, and ultimately alleviate dysphagia symptoms.

According to the principle of initial values, subjects with a lower initial physiological capacity have a greater potential to improve. For example, women with lower initial values in hip abductor strength, power, and stability have greater changes following resistance and jump training than those with higher initial values (Winters-Stone & Snow, 2003). Similarly, when documenting the effects of EMST training on maximal expiratory pressure in people with MS, compared to healthy controls, the results indicated that people with MS had more relative gains following training in comparison to healthy controls. The difference in maximum expiratory pressure from pre-training to post-training for the MS group was 40.4% whereas for healthy controls the difference was 29%, however this difference in gains was not statistically different (Chiara, Martin, & Sapienza, 2007). Changes in strength of the muscles involved in swallowing following training have not been compared between PD and healthy subjects.

The need for improved health services for Parkinson's disease

Current clinical practice in providing appropriate speech therapy services to individuals with PD is lacking both in availability and in dysphagia management techniques. A United Kingdom survey revealed that the main focus of dysphagia intervention for PD patients was on techniques that modify texture and consistency, with no application of exercise techniques (Miller, Deane, Jones, Noble, & Gibb, 2010). In New Zealand, interviews of 500 people with PD shed light on several unmet needs of this population. One of them was access to non-medical providers of health care, and in particular speech and language therapists were seen less often than desired (Buetow, Giddings, Williams, & Nayar, 2008).

There is a need to develop and explore targeted training techniques for PD patients with dysphagia, and make those available for clinical use. Training programmes emphasizing a skill component are often used in physiotherapy and occupational therapy for upper-limb rehabilitation in this population (Morris et al., 2010; Platz et al., 1998; Rostami & Ashayeri, 2009). There is support for implementing frequent external cues in rehabilitation programs for improving motor function, which might be also be relevant for swallowing rehabilitation in individuals with dysphagia secondary to PD. In addition, specific speech therapy (i.e., LSVT) is offered to meet the unique needs of individuals with a speech disorder secondary to PD (Ramig et al., 2001). However, the lack of specific swallowing therapy for this population should be addressed. Perhaps making such a therapy available would change practice, and clinicians will have a better choice than compensatory techniques.

Skill training in Parkinson's disease

As mentioned (Section 8.1), data for the current pilot study were collected in conjunction with a Master's project. The supervision team for this project included the PhD candidate. The following is a short description of the study's procedure and results.

Ten individuals with dysphagia secondary to PD (see Table 8.1 for patient demographics) went through 2 weeks (10 sessions) of swallowing skill training with immediate feedback. The assessments included the Timed water swallow test (Hughes & Wiles, 1996), Test of mastication and swallowing of solids (TOMASS) (unpublished data), submental and masseter sEMG, CSA of the submental muscle measured by ultrasonography, hyoid movement measured by ultrasonography, and swallowing quality of life questionnaire (SWAL-QOL) (McHorney, Bricker, Robbins, et al., 2000; McHorney, Bricker, Kramer, et al., 2000). Table 8.3 presents the timetable for this study.

The results of the study indicated shorter pre-motor time and in pre-swallow time in non-effortful swallowing tasks of saliva and 10 mL water following swallowing SKL-I training. Pre-motor time was defined as the time gap between the onset of the sEMG signal and its peak, and pre-swallow time was defined as the time difference between the first change in the waveform to the onset of swallowing. Reduced pre-motor and pre-swallow time following SKL-I training indicates faster execution of swallowing. In addition, improvements were found in the water swallowing test following SKL-I training with increase volume (mL) per swallow and decreased time per swallow. The duration of the sEMG signal from the submental muscle group in non-effortful saliva swallowing shortened. Overall, these results reflected improved efficiency in swallowing. The SWAL-QOL questionnaire also suggested improvements following training. The CSA, hyoid displacement, and TOMASS did not change (Athukorala, 2012).

This current study investigated several further questions regarding the subjects' data, focusing on sEMG peak amplitude and motor performance during training.

8.3 Hypotheses

8.3.1 Changes in submental muscle group activity following SKL-I training

8.3.1.1 SKL-I training effects in the dysphagic group

Unresolved question

Are there changes in submental muscle activity following swallowing skill training in individuals with dysphagia secondary to PD?

Hypothesis

Individuals with dysphagia secondary to PD will have increased peak activity of the submental muscle group during non-effortful swallowing tasks (saliva swallowing and water swallowing) and in effortful tasks (saliva swallowing and water swallowing).

Rationale

Similar to the rationale presented in *Chapter 4*, skill training will result in increased submental activity in non-effortful swallowing tasks, which may indirectly reflect efficient firing pattern of the submental motoneurons during the trained task (which is essentially non-effortful swallowing

of saliva). This improvement will occur according to the principle of task specificity that states that performance will improve if the training consists of the activity itself (Barnett et al., 1973; Ranganathan & Newell, 2010; Rushall & Pyke, 1990). Transference from the practice task to a bolus swallowing task (non-effortful 10 mL water) may occur due to the similarity between the two tasks that would lead to a carryover effect (Burkhead et al., 2007).

In addition, improved neural control over, and increased efferent downflow to, the submental muscles is expected to be reflected during the execution of effortful swallowing tasks as increased peak amplitude. Increased peak amplitude may indirectly reflect improved firing synchronization, increased firing rate, and recruitment of additional motor units (Shinohara & Søgaard, 2006; Staudenmann et al., 2010). Transference to a non-practised task of effortful swallowing in individuals with dysphagia secondary to PD is expected to appear based upon a link between functional improvement and increase strength in individuals with PD (Falvo et al., 2008)

Significance

If proven, swallowing skill training will help alleviate dysphagia symptoms in patients with PD, hence improving their quality of life.

Proposed study

Four types of tasks will be used: saliva swallowing and 10 mL water swallowing (non-effortful tasks) and effortful saliva swallowing and 10 mL water swallowing (effortful tasks). Measurements will be taken at 2 weeks before training, 4 days before training, 3 days after a 2-week training period, and 2 weeks after the training was completed.

8.3.1.2 *Dysphagic vs. non-dysphagic: effects of SKL-I training*

Unresolved question

Are there differences between individuals with dysphagia secondary to PD and healthy subjects in the change in the submental muscle group activity following swallowing skill training?

Hypothesis

Individuals with dysphagia secondary to PD will have a larger increase in the peak amplitude of submental activity following skill training than healthy subjects.

Rationale

The effects of EMST were examined in individuals with MS with mild-moderate level of motor disability in comparison to healthy controls. People with MS had greater gains (percent change from baseline) in maximum expiratory pressure in comparison to the gains of healthy controls (Chiara et al., 2007). Similarly, individuals with dysphagia secondary to PD will have greater capacity for changes following training, than healthy subjects.

Significance

Differences in extent of improved swallowing function following training will indicate if individuals with dysphagia secondary to PD have changes similar to, lower than, or greater than those of healthy non-dysphagic individuals. It is important to identify differences in gains following training, as they can influence the interpretations of the data when comparing non-dysphagic individuals to dysphagic individuals when studying the influences of swallowing training.

Proposed study

For the dysphagic group and the non-dysphagic group, peak amplitude of submental sEMG will be measured during the two non-effortful swallowing tasks and the two effortful swallowing tasks. In the dysphagic group, baseline measurements will be taken twice, 9 days apart, at 2 weeks and at 4 days prior to training, and outcome measures will be taken twice, at 3 days and at 2 weeks post training. The results taken in the two time points before training will be averaged. In the non-dysphagic group, measurement will be taken once, at 3-12 days prior to training and outcome measures will be taken once, at 4 days post training. In order to compare relative changes following training, percent change between pre-training measurements and post-training measurement will be calculated for each task, and for each group.

8.3.1.2.1 *Dysphagic vs. non-dysphagic: baseline differences*

Unresolved question

To answer the question regarding the differences in submental activity changes following SKL-I training between dysphagic and non-dysphagic subjects, another question has to be asked. Are there differences between individuals with dysphagia secondary to PD and healthy subjects in absolute level of submental muscle group activity? Answering this secondary question can clarify differences, if any, in the changes following training between the two subject groups.

Hypothesis

Individuals with PD and dysphagia will have lower amplitude peak of submental activity at baseline than healthy subjects.

Rationale

As mentioned before, EMST was found the cause greater gains (percent change from baseline) in maximum expiratory pressure in individuals with MS in comparison to healthy controls (Chiara et al., 2007). A possible explanation might be due to lower initial values in the MS group that allowed for more 'room' for change.

Significance

Specifically to the submental muscles, there are no reports in the literature regarding the sEMG peak amplitude in PD patients with or without dysphagia, thus the baseline values needs to be tested by comparing submental peak amplitude between individuals with and dysphagia PD and healthy controls.

Proposed study

For the dysphagic group and the non-dysphagic group, peak amplitude of submental sEMG will be measured during saliva swallowing and 10 mL water swallowing (non-effortful tasks) and effortful saliva swallowing and 10 mL water swallowing (effortful tasks). In the PD group, baseline measurements will be taken at 2 weeks before training and 4 days before training. The results taken in the two time points before training will be averaged. In the non-dysphagic group, measurement will be taken 4 days before training. In order to compare initial values, the raw data at baseline measurement will be compared.

8.3.2 Participants' performance during swallowing training

8.3.2.1 Changes in motor performance during training in the dysphagic group

Unresolved question

Are there changes in motor performance (target hit-rate) during swallowing skill training with immediate feedback in individuals with dysphagia secondary to PD?

Hypothesis

Individuals with dysphagia secondary to PD will have an increase in motor performance (target hit rate) over the course of training.

Rationale

During learning, individuals with dysphagia secondary to PD will be able to use the immediate visual feedback to enhance motor planning of swallowing. A study that compared two feedback protocols: 100% knowledge of results to 20% knowledge of results in individuals with PD, found that in the 100% protocol, individuals with PD had better performances than in the low feedback frequency protocol (Guadagnoli et al., 2002).

Significance

The same study mentioned above also found that on retention task, individuals with PD that received 100% feedback, performed better than individuals with PD in the 20% feedback protocol, and similar to healthy controls (Guadagnoli et al., 2002). Similarly, if individuals with PD can benefit from high frequency visual feedback during training, they might improve in functional swallowing.

Proposed study

Participants' performance (target hit-rate) during skill training will be recorded.

8.3.2.2 *Dysphagic vs. non-dysphagic: differences in motor performance*

Unresolved question

Are there differences between individuals with dysphagia secondary to PD and healthy subjects in the change of performance (target hit-rate) during swallowing skill training with immediate feedback?

Hypothesis

Unlike healthy subjects, individuals with dysphagia secondary to PD will present lower increases in target hit-rate during swallowing skill training.

Rationale

Individuals with PD have difficulties in organizing movements into a sequence due to dysfunction of the BG affecting the SMA (Cunnington et al., 1997; Harrington & Haaland, 1991). Although

this difficulty might not affect performance of simple movements (Cunnington et al., 1997), it can affect the execution of complex motor movement, like swallowing. Swallowing-skill training aims to increase precision of movement during swallowing. Since accuracy is dependent on creating an organized motor plan, individuals with PD will have decreased accuracy in comparison to healthy subjects due to the BG dysfunction in PD (Cunnington et al., 1995, 1997; Hanna-Pladdy & Heilman, 2010).

Significance

Achievement of an increased hit-rate during the course of skill training can assist in interpretation of the other outcome measures. If the subjects did achieve the training goal, then the other outcome measures can be evaluated in light of fulfilment of the training goal. However, if the goal was not achieved, then the lack of changes following training may be related to poor task execution. In addition, assessing performance throughout training can help in identifying a need for designing a better/different protocol for training.

Proposed study

Performance (target hit-rate) during skill training with immediate feedback recorded during training will be compared between individuals with PD and dysphagia to that of healthy subjects.

8.4 Methodology

8.4.1 Participants

8.4.1.1 Dysphagic group

Ten patients (three females and seven males; mean age \pm SD: 67.4 \pm 8.6 years; age range: 54–84 years) with dysphagia secondary to PD were recruited for the study. Patients demographics (age, gender, onset of PD [time of diagnosis], Hoehn & Yahr score, reported swallowing difficulties by the patient, and other medical conditions reported by the patient) are presented in Table 8.1. Overall, the time post onset of PD ranged 2–16 years (mean \pm SD 6.7 \pm 3.9 years), the time post onset of swallowing difficulties ranged 7–36 months (mean \pm SD 24 \pm 11.7 month), and Hoehn & Yahr score (Hoehn & Yahr, 1967) for PD severity ranged 2–3 points (mean 2.5 points).

Patients were recruited through the Van der Veer Clinic for Parkinson's Disease (Christchurch, NZ), the New Zealand Brain Research Institute database, the Parkinsonism Society of New Zealand, and Canterbury District Health Board (CDHB) hospitals. Each recruitment centre was provided the Eating Assessment Tool (EAT-10) (Belafsky et al., 2008) which is a self-administered questionnaire related to dysphagia symptoms (Appendix 9). Patients with PD attending these centres were offered a questionnaire. In addition, an advertisement was placed in a newsletter of the Parkinsonism Society of New Zealand. Patients who identified themselves as having swallowing difficulties due to PD, were contacted by the researcher.

Interested participants were provided with a detailed information sheet (Appendix 10). After making sure that the inclusion/exclusion criteria were met, the first appointment at the Swallowing Rehabilitation Research Laboratory located at the New Zealand Brain Research Institute (NZBRI) in Christchurch was scheduled. During the first appointment, the research project was discussed and time was given for questions and clarifications as needed. The relevant measurement tools were introduced and the participants completed a questionnaire that detailed the inclusion criteria (Appendix 11). Participants then gave informed consent (Appendix 12) and the first baseline session was conducted. Participants were not given compensation for study participation.

Exclusion criteria

Exclusion criteria included Parkinsonism not caused by PD (e.g., multiple system atrophy progressive supranuclear palsy, side effects of medications (such as some antipsychotics), history of neurological disorder (e.g., stroke, dementia), history of muscular disorder, and/or history of head and/or neck surgery or injury). In addition, the participants were asked to report on a history of gastroesophageal reflux disease (GERD). In case of such reports, the researcher further enquired regarding the severity and past interventions, specifically surgery. Participants were included if no surgical procedure had been conducted and symptoms were considered well controlled.

Inclusion criteria

Recruited participants met all of the following inclusion criteria: PD as diagnosed by a neurologist, existing swallowing difficulties as reported by the patient had been present for at least 2 months, and the presence of dysphagia in clinical swallowing examination, conducted by a member of the research team. Medication for PD was continued as normally prescribed.

Discontinuation

One participant discontinued the study due to scheduling difficulties, and was replaced by another participant.

This study was approved by the Upper South B Regional Ethics Committee, New Zealand.

Table 8.1 Patients demographics: age, gender, onset of Parkinson's disease (time of diagnosis) in years, dysphagia onset (in month) Hoehn & Yahr (H-Y) score, reported swallowing difficulties by the patient, and other medical conditions reported by the patient

Age	Gender	PD onset (y)	Dysphagia onset (m)	H-Y score	Reported swallowing difficulties	Other medical conditions reported
84	Male	6	36	3	Coughs on food & liquid Takes long time to chew Food sticking in mouth & throat Drooling	Depression Heart condition
76	Male	10	36	3	Loss of weight Difficulty swallowing pills Long time to chew Food sticking on mouth & throat	High blood pressure Foot neuroma Skin carcinoma Mild cognitive impairments
71	Female	16	10	3	Difficulty swallowing solids>liquids Coughs on food & liquid Food sticking in mouth & throat Uses straw to drink liquid	Arthritis High blood pressure Ptosis of both eyes
69	Male	7	36	3	Coughs on liquid & food Food sticking in mouth & throat Drooling	Scoliosis
66	Male	2	11	2	Coughs on food & liquid Food sticking in mouth & throat	High blood pressure Heart condition

66	Female	6	12	3	Struggle to swallow Coughs on food & liquid Food sticking in mouth & throat Drinks thickened liquid Pain while swallowing	Osteoarthritis Polymyalgia (muscle pain) Depression Hiatus hernia
67	Male	5	7	2	Difficulty swallowing pills Cough on liquid	High cholesterol Diabetes Asthma
64	Male	4	24	2	Food sticking in mouth & throat Difficulty swallowing pills Coughs on liquid>solids, Drooling	H/o Prostate cancer, High blood pressure High cholesterol Mild cognitive impairments
57	Female	3	36	2	Difficulty swallowing solids>liquids Loss of weight Longer time to chew Eating is un-pleasurable Uses bottle/straw	Diabetes (type 2) High cholesterol Osteopenia (low bone density) Mild cognitive impairments
54	Male	7	24	2	Food sticking in mouth & throat Needs to swallow hard to get food down	High blood pressure Cholesterol H/o heart attack Depression

8.4.1.2 *Non-dysphagic group*

Data from ten healthy participants who took part in the main study (Chapter 5 and 6) were included in this study. All took part in SKL-I training. Age and gender are presented in Table 8.2.

Table 8.2 *Ages (mean \pm SD, range in brackets) and number of subjects (n), in the skill-immediate group (n=10)*

<i>Age group</i>	<i>Gender</i>	<i>Skill-immediate</i>
Young	Female	24.6 \pm 4.7 (21-30) n = 3
	Male	25.5 \pm 6.3 (21, 30) n = 2
Old	Female	63 \pm 5.6 (59,67) n = 2
	Male	73 \pm 10.4 (67-85) n = 3

8.4.2 *Instrumentation*

The instruments used for this study are presented in Chapter 5 - Assessment and Training Methods:

- EMG instrumentation for submental sEMG: see Section 5.2.3.
- BiSSkiT software for swallowing training: see Section 5.3.1 (software design), Section 5.3.2 (software application), and Section 5.3.2.2 (skill training - immediate feedback).

8.4.3 Procedure

Participants attended the Swallowing Rehabilitation Research Laboratory located at the New Zealand Brain Research Institute where all the assessment and training sessions took place. Each participant was seen individually. All assessments and training sessions were completed during the ‘On’ phase of the PD's medication, thus these were scheduled around the time of their best performance, generally within one hour of medication consumption. Table 8.3 presents the timetable of measurements taking.

Each participant was seen for 14 sessions. The initial session included the 1st baseline session and was carried out 2 weeks prior to the first swallowing training session. The 2nd baseline session was carried out 3 or 4 days prior to the 1st training session. The following training sessions (2–10) took place every consecutive day, excluding the weekend (Saturday and Sunday). Training was provided 1 hour a day, 5 days a week, for 2 weeks, and focused on swallowing precision. Surface EMG biofeedback utilizing custom-designed software (BiSSkiT software) to facilitate mastery of training goals was used. Training was given individually and all training sessions were monitored by the Master's student. Three days after the 10th training session (i.e., Monday), the first outcome session was carried out. Two weeks after the 10th training session, the second outcome session was carried out. Both outcome sessions included the same assessments that were taken at the baseline sessions in order to document the cumulative outcomes of the training on the biomechanical and muscular levels.

Table 8.3 Timetable of appointments at the laboratory, including the measurements taken

Session name	Time	Measurements taken
1 st baseline session	2 weeks prior to 1 st training session	<ul style="list-style-type: none"> - Clinical swallowing assessment - Water swallow test - TOMASS - Submental and masseter sEMG - Ultrasound: submental CSA & hyoid movement

		- SWAL-QOL
2 nd baseline session	3-4 days prior to 1 st training session	- Water swallow test - TOMASS - Submental and masseter sEMG - Ultrasound: submental CSA & hyoid movement - SWAL-QOL
Training sessions:	Week 1: Monday-Friday Week 2: Monday-Friday	- 1 st – 10 th training sessions (target hit rate)
1 st outcome session	3 days following the last (10 th) training session	- Water swallow test - TOMASS - Submental and masseter sEMG - Ultrasound: submental CSA and hyoid movement - SWAL-QOL
2 nd outcome session	2 weeks following the last (10 th) training session	- Water swallow test - TOMASS - Submental and masseter sEMG - Ultrasound: submental CSA and hyoid movement - SWAL-QOL

Table 8.4 presents the assessment and training procedure relevant to the current study. Details regarding the procedure for the assessments reported in the current chapter are provided in Section 5.4.6 – *sEMG procedure*, and Section 5.5.1 - *Swallowing training*.

Table 8.4 PD training and assessment protocol

	Baseline 1*	Baseline 2**	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6	Session 7	Session 8	Session 9	Session 10	Outcome 1***	Outcome 2****
Submental sEMG	5 non-effortful saliva	5 non-effortful saliva											5 non-effortful saliva	5 non-effortful saliva
	5 non-effortful 10 mL	5 non-effortful 10 mL											5 non-effortful 10 mL	5 non-effortful 10 mL
	5 effortful saliva	5 effortful saliva											5 effortful saliva	5 effortful saliva
	5 effortful 10 mL	5 effortful 10 mL											5 effortful 10 mL	5 effortful 10 mL
Performance: hit rate			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Performance: sEMG peak			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		

* 2 weeks prior to 1st training session

** 3-4 days prior to 1st training session

*** 3 days after the 10th training session

**** 2 weeks after the 10th training session

8.4.4 Data extraction

See Section 5.7.3 – sEMG data, and section 5.7.6 – Training performance: sessions' hit rate and each session mean peak amplitude from sEMG electrodes placed at the submental muscle area.

8.4.5 Statistical analysis

Statistical analyses were conducted using SPSS statistics package (IBM SPSS Statistics version 19.0). When the research question focused on differences over time in one group, RM-ANOVA was used (e.g., 1st baseline, 2nd baseline, 1st outcome, 2nd outcome). When the research questions focused on differences between the groups over time, 'mixed' design ANOVA was used (within- and between-subjects analysis). Post hoc analysis was conducted when appropriate.

When measuring training effects in the PD group, each analysis included RM-ANOVA with TIME as a within group factor and two covariates: onset of PD (as diagnosed by a neurologist) and onset of dysphagia (as subjectively reported by the patient). These covariates were entered to the model since the motor deficits associated with PD might influence the sEMG peak amplitude, and in addition, the PD group was composed of patients that differ from each other in these independent variables.

When comparing the changes following training between the PD group (Dysphagic) to the healthy group (Non-dysphagic group), the percent change from baseline to post-training measurement was the dependent variable, GROUP was a between-groups factor (Dysphagic vs. Non-dysphagic), and AGE (in years) was entered to the model as a covariate, since the PD group was composed of older subjects only, but the healthy group was composed of younger and older subjects.

When comparing baseline values between the groups, the baseline value was the depended variable, GROUP was a between-groups factor (Dysphagic vs. Non-dysphagic), and AGE (in years) was entered as a covariate.

Testing for changes in submental activity included four analyses: for effortful saliva, effortful 10 mL water, non-effortful saliva, and for non-effortful 10 mL water swallowing.

Sphericity was tested when three or more components (e.g., time points) were entered into the ANOVA model. In case sphericity was violated, Greenhouse-Geisser correction for degrees of freedom was applied. Equality (homogeneity) of variance was tested for using Leven's test when between-groups factors were tested.

Significance value was set at $\alpha \leq 0.05$. All tests were two-sided. Post hoc analysis was conducted when the model showed significant results. Marginally significant results were defined as $0.05 < \alpha \leq 0.10$. Correction for multiple comparisons was not applied due the exploratory nature of this study (Nakagawa, 2004; Phillips, 2004; Robey, 2004a). Confidence intervals (*CI*) are reported as 95% *CI* around the mean difference or around the mean, and appear in the text as *CI*.

8.5 Results

8.5.1 *Changes in submental muscle group activity following SKL-I training*

8.5.1.1 *SKL-I training effects in the Dysphagic group*

Is there an effect of SKL-I training on submental muscle activity as measured by sEMG in the Dysphagic group?

Effortful saliva swallowing task

One-factor RM-ANOVA with TIME (1st baseline, 2nd baseline, 1st outcome, 2nd outcome) with dysphagia onset (in years) and PD onset (in years) as covariates was conducted in the PD group. There was a significant effect of TIME ($F(3, 21) = 4.48, p = 0.01$). There were no significant effects of TIME*DYSPHAGIA ONSET ($F(3, 21) = 2.25, p = 0.11$), and TIME*PD ONSET ($F(3, 21) = 1.96, p = 0.15$).

Post hoc analysis revealed a significant effect when comparing baseline 1 to outcome 2 ($F(1, 7) = 8.56, p = 0.02$). No significant effects of TIME were found when comparing baseline 1 to baseline 2 ($F(1, 7) = 1.14, p = 0.32$), baseline 2 to outcome 1 ($F(1, 7) = 1.73, p = 0.23$), outcome 1 to outcome 2 ($F(1, 7) = 2.70, p = 0.14$), and baseline 2 to outcome 2 ($F(1, 7) = 4.42, p = 0.07$).

Table 8.5 sEMG peak amplitude (μV): effortful saliva swallowing task - estimated means, standard deviation and 95% CI around the mean

	Mean	SD	CI
Baseline 1	76.8	42.8	44.9, 108.6
Baseline 2	85.6	41.3	53.6, 117.6
Outcome 1	85.8	28.7	61.6, 109.9
Outcome 2	92.4	44.5	55.7, 129.1

Table 8.6 Changes over time (μV): sEMG during effortful saliva swallowing: estimated mean difference between assessment 95% CI for the mean difference, and Cohen's *d* (B1 - baseline 1, B2 - baseline 2, O1 - outcome 1, O2 - outcome 2)

Times compared	Mean difference	95% CI for the mean difference	Cohen's <i>d</i>
Baseline 1 vs. baseline 2	8.8 (B2 > B1)	-5.6, 23.2	0.22
Baseline 2 vs. outcome 1	0.2 (O1 > B2)	-25.8, 26.2	0.01
Outcome 1 vs. outcome 2	6.6 (O2 > O1)	-10.6, 23.9	0.19
Baseline 2 vs. outcome 2	6.8 (O2 > B2)	-22.9, 36.6	0.17
Baseline 1 vs. outcome 2	15.6 (O2 > B1)	-11.1, 42.2	0.38

Effortful 10 mL water swallowing task

One-factor RM-ANOVA with TIME, and dysphagia onset and PD onset as covariates was conducted in the PD group. There was a significant effect of TIME ($F(3, 21) = 3.33, p = 0.04$). There were no significant effects of TIME*DYSPHAGIA ONSET ($F(3, 21) = 2.18, p = 0.12$), and TIME*PD ONSET ($F(3, 21) = 1.19, p = 0.33$). Post hoc analysis revealed a marginally significant effect of TIME when comparing baseline 1 to outcome 2 ($F(1, 7) = 5.04, p = 0.053$). There were no significant effects when comparing baseline 2 to outcome 1 ($F(1, 7) = 1.55, p = 0.25$), baseline 1 to baseline 2 ($F(1, 7) = 0.39, p = 0.55$), baseline 2 to outcome 2 ($F(1, 7) = 4.34, p = 0.076$), or outcome 1 to outcome 2 ($F(1, 7) = 1.87, p = 0.21$).

Table 8.7 sEMG peak amplitude (μV): effortful water swallowing task - estimated means, standard deviation and 95% CI around the mean

	Mean	SD	CI
Baseline 1	81.8	43.6	49.6, 114.1
Baseline 2	84.6	43.1	51.2, 117.9
Outcome 1	87.4	36.9	56.2, 118.5
Outcome 2	92.2	58.2	43.7, 140.7

Table 8.8 Changes over time (μV): sEMG during effortful water swallowing: estimated mean difference between assessment 95% CI for the mean difference, and Cohen's d (B1 - baseline 1, B2 - baseline 2, O1 - outcome 1, O2 - outcome 2)

Times compared	Mean difference	95% CI for the mean difference	Cohen's d
Baseline 1 vs. baseline 2	2.7 (B2 > B1)	-13.7, 19.2	0.07
Baseline 2 vs. outcome 1	2.8 (O1 > B2)	-19.4, 24.9	0.07
Outcome 1 vs. outcome 2	4.8 (O2 > O1)	-20.2, 29.9	0.10
Baseline 2 vs. outcome 2	7.6 (O2 > B2)	-22.1, 37.3	0.16
Baseline 1 vs. outcome 2	10.2 (O2 > B1)	-20.7, 41.4	0.21

Non-effortful saliva swallowing task

One-factor RM-ANOVA with TIME, and dysphagia onset and PD onset as covariates was conducted in the PD group. There was a significant effect of TIME*DYSPHAGIA ONSET ($F(3, 21) = 4.32, p = 0.016$). There were no significant effects of TIME ($F(3, 21) = 2.20, p = 0.11$) or TIME*PD ONSET ($F(3, 21) = 1.06, p = 0.38$).

Post hoc analysis revealed that TIME*DYSPHAGIA ONSET was significant when comparing baseline 1 to baseline 2 ($F(1, 8) = 8.49, p = 0.02$), and baseline 1 to outcome 2 ($F(1, 8) = 7.08, p = 0.03$). However, there were no significant effects when comparing baseline 2 to outcome 1 ($F(1, 8) = 0.48, p = 0.50$), outcome 1 to outcome 2 ($F(1, 8) = 0.01, p = 0.91$), or baseline 2 to outcome 2 ($F(1, 8) = 0.05, p = 0.83$).

A linear regression analysis was conducted to explore the relationship between dysphagia onset and sEMG amplitude in this task. With every year of an increase in dysphagia onset there was a decrease of 12.5 μV (SE of B : 4.3, β : -0.72, CI [-22.4, -2.6]) in the difference between baseline 2 to baseline 1 (baseline 2 *minus* baseline 1, Constant: 20.1, CI [-1.2, 41.6]) ($F(1, 8) = 8.49, p =$

0.02, R^2 adj = 0.45). With every year of an increase in dysphagia onset there was a decrease of 11.6 μ V (SE of B : 4.36, β : -0.68, CI [-21.7, -1.5]) in the difference between outcome baseline 1 and outcome 2 (outcome *minus* baseline. Constant: 19.8, CI [-1.9, 41.6], i.e., with every year increase in dysphagia onset, there is a decrease from baseline to outcome) ($F(1, 8) = 7.08$, $p = 0.03$, R^2 adj = 0.40).

Table 8.9 sEMG peak amplitude (μ V): non-effortful saliva swallowing task - estimated means, standard deviation and 95% CI around the mean

	Mean	SD	CI
Baseline 1	52.0	22.3	36.9, 67.1
Baseline 2	47.9	20.1	31.4, 64.5
Outcome 1	43.4	15.7	30.2, 56.6
Outcome 2	49.3	23.1	30.9, 67.8

Table 8.10 Changes over time: sEMG (μ V) during non-effortful saliva swallowing: estimated mean difference between assessment 95% CI for the mean difference, and Cohen's d (B1 - baseline 1, B2 - baseline 2, O1 - outcome 1, O2 - outcome 2)

Times compared	Mean difference	95% CI for the mean difference	Cohen's d
Baseline 1 vs. baseline 2	4.05 (B1 > B2)	-6.0, 14.1	0.20
Baseline 2 vs. outcome 1	4.5 (B2 > O1)	-0.8, 9.9	0.26
Outcome 1 vs. outcome 2	5.9 (O2 > O1)	-2.6, 14.6	0.31
Baseline 2 vs. outcome 2	1.4 (O2 > B2)	-8.3, 11.1	0.07
Baseline 1 vs. outcome 2	2.6 (B1 > O2)	-8.1, 13.4	0.12

Non-effortful 10 mL water swallowing task

One-factor RM-ANOVA with TIME, and dysphagia onset and PD onset as covariates was conducted in the PD group. There were no significant effects of TIME ($F(3, 21) = 0.42$, $p = 0.74$), TIME*PD ONSET ($F(3, 21) = 0.29$, $p = 0.82$), or TIME*DYSPHAGIA ONSET ($F(3, 21) = 0.94$, $p = 0.43$).

Table 8.11 sEMG peak amplitude (μV): non-effortful water swallowing task - estimated means, standard deviation and 95% CI around the mean

	Mean	SD	CI
Baseline 1	50.8	18.6	35.7, 65.8
Baseline 2	44.7	21.7	26.7, 62.7
Outcome 1	44.6	18.1	29.5, 59.8
Outcome 2	46.7	24.9	25.6, 67.8

Table 8.12 Changes over time: sEMG (μV) during non-effortful water swallowing: estimated mean difference between assessment 95% CI for the mean difference, and Cohen's d (B1 - baseline 1, B2 - baseline 2, O1 - outcome 1, O2 - outcome 2)

Times compared	Mean difference	95% CI for the mean difference	Cohen's d
Baseline 1 vs. baseline 2	6.1 (B1 > B2)	-7.5, 19.8	0.32
Baseline 2 vs. outcome 1	0.1 (B2 > O1)	-8.1, 8.2	0.01
Outcome 1 vs. outcome 2	2.0 (O2 > O1)	-7.7, 11.8	0.10
Baseline 2 vs. outcome 2	1.9 (O2 > B2)	-6.9, 10.8	0.09
Baseline 1 vs. outcome 2	4.1 (B1 > O2)	-8.5, 16.8	0.20

8.5.1.1.1 Summary

Following training, there was a significant increase in sEMG peak amplitude in the effortful saliva swallowing task and a marginally significant increase in the effortful 10 mL water swallowing task in the Dysphagic group. However, the effect size for these increases was small.

In the non-effortful saliva swallowing task, there was an interaction between the onset of dysphagia symptoms and the magnitude of sEMG peak amplitude over the time of evaluation, with a negative relationship between the two. In the non-effortful water swallowing task, no significant effects were detected.

8.5.1.2 Dysphagic vs. Non-dysphagic: effects of SKL-I training

Are there differences between the Dysphagic and Non-dysphagic groups in changes of submental muscle peak amplitude as measured by sEMG following SKL-I training?

Effortful saliva swallowing task

There was no significant effect of GROUP ($F(1, 17) = 1.01, p = 0.33$). The effect of AGE was marginally significant ($F(1, 17) = 3.29, p = 0.09$). Taking into account AGE as covariate, the difference between the groups was 28.8% (Non-dysphagic < Dysphagic, $CI [-31.7, 89.4]$, Cohen's $d = 0.51$). The Non-dysphagic group had an estimated mean of 103.0% change ($CI [63.1, 142.9]$), and the Dysphagic group had an estimated mean of 131.9% change ($CI [91.9, 171.8]$).

Effortful 10 mL water swallowing task

There was no significant effect of GROUP ($F(1, 17) = 1.74, p = 0.20$), or AGE ($F(1, 17) = 2.56, p = 0.13$). Taking into account AGE as covariate, the difference between the groups was 28.2% (Non-dysphagic < Dysphagic, $CI [-16.8, 73.2]$, Cohen's $d = 0.70$). The Non-dysphagic group had an estimated mean of 91.9% change ($CI [62.2, 121.6]$), and the Dysphagic group had an estimated mean of 120.1% change ($CI [90.3, 149.8]$).

Non-effortful saliva swallowing task

There was no significant effect of GROUP ($F(1, 17) = 1.04, p = 0.32$). The effect of AGE was marginally significant ($F(1, 17) = 3.48, p = 0.08$). Taking into account AGE as covariate, the difference between the groups was 19.2% (Non-dysphagic > Dysphagic, $CI [-20.5, 58.9]$, Cohen's $d = 0.55$). The Non-dysphagic group had an estimated mean of 122.0% change ($CI [95.8, 148.2]$), and the Dysphagic group had an estimated mean of 102.7% change ($CI [76.6, 128.9]$).

Non-effortful 10 mL water swallowing task

There was no significant effect of GROUP ($F(1, 17) = 0.06, p = 0.80$). The effect of AGE was marginally significant ($F(1, 17) = 3.65, p = 0.07$). Taking into account AGE as covariate, the difference between the groups was 4.7% (Non-dysphagic > Dysphagic, $CI [-43.9, 34.4]$, Cohen's $d = 0.14$). The Non-dysphagic group had an estimated mean of 109.4% change ($CI [83.5, 135.2]$), and the Dysphagic group had an estimated mean of 104.6% change ($CI [78.7, 130.4]$).

8.5.1.2.1 Summary

There were no significant differences between the Dysphagic and Non-dysphagic groups in the changes in submental activity (sEMG peak amplitude) following SKL-I training in effortful and non-effortful swallowing tasks.

8.5.1.3 Dysphagic vs. Non-dysphagic: baseline differences

Are there differences between the Dysphagic and Non-dysphagic groups in baseline measurements of submental activity as measured by sEMG peak amplitude?

Effortful saliva swallowing task

There was a significant effect of GROUP ($F(1, 17) = 5.95, p = 0.03$). There was no significant effect of AGE ($F(1, 17) = 0.00, p = 0.95$). Taking into account AGE as covariate, the difference between the groups was 73.4 μV (Non-dysphagic > Dysphagic, $CI [9.9, 136.9]$, Cohen's $d = 1.37$). The Non-dysphagic group had an estimated mean of 154.1 μV ($CI [112.3, 196.0]$), and the Dysphagic group had an estimated mean of 80.7 μV ($CI [38.8, 122.6]$).

Effortful 10 mL water swallowing task

There was a significant effect of GROUP ($F(1, 17) = 9.00, p = 0.01$). There was no significant effect of AGE ($F(1, 17) = 0.05, p = 0.83$). Taking into account AGE as covariate, the difference between the groups was 74.5 μV (Non-dysphagic > Dysphagic, $CI [22.1, 126.9]$, Cohen's $d = 1.71$). The Non-dysphagic group had an estimated mean of 156.4 μV ($CI [121.8, 190.9]$), and the Dysphagic group had an estimated mean of 81.8 μV ($CI [47.3, 116.4]$).

Non-effortful saliva swallowing task

There were no significant effects of GROUP ($F(1, 17) = 0.01, p = 0.94$), or AGE ($F(1, 17) = 0.11, p = 0.74$). Taking into account AGE as covariate, the difference between the groups was 0.77 μV (Non-dysphagic < Dysphagic, $CI [-21.1, 22.6]$, Cohen's $d = 0.05$). The Non-dysphagic group had an estimated mean of 48.4 μV ($CI [33.9, 62.8]$), and the Dysphagic group had an estimated mean of 49.1 μV ($CI [34.7, 63.5]$).

Non-effortful 10 mL water swallowing task

There were no significant effects of GROUP ($F(1, 17) = 0.03, p = 0.86$), or AGE ($F(1, 17) = 0.01, p = 0.91$). Taking into account AGE as covariate, the difference between the groups was 1.81 μV (Non-dysphagic < Dysphagic, $CI [-18.9, 22.6]$, Cohen's $d = 0.11$). The Non-dysphagic group had an estimated mean of 45.6 μV ($CI [31.9, 59.3]$), and the Dysphagic group had an estimated mean of 47.4 μV ($CI [33.8, 61.2]$).

8.5.1.3.1 Summary

When comparing submental sEMG peak amplitude measurements at baseline between Dysphagic and Non-dysphagic, Non-dysphagic had higher sEMG peak amplitude than Dysphagic in effortful swallowing tasks, but not in non-effortful swallowing tasks.

8.5.2 Participants' performance during swallowing training

8.5.2.1 Changes in motor performance during training in the Dysphagic group

Are there changes in target hit-rate during swallowing SKL-I training in the Dysphagic group?

RM-ANOVA with TIME (sessions 1-10) as a within-group factor and PD onset and dysphagia onset as covariates was conducted in the Dysphagic group. There were no significant effects of TIME ($F(4.10, 28.7) = 0.76, p = 0.55$), TIME*PD ONSET ($F(4.10, 28.7) = 0.35, p = 0.84$), or TIME*DYSPHAGIA ONSET ($F(4.10, 28.7) = 0.85, p = 0.51$).

8.5.2.2 Dysphagic vs. Non-dysphagic: differences in motor performance

Are there differences in target hit-rate changes during SKL-I training between the Dysphagic and Non-dysphagic groups?

Two-factor mixed ANOVA was conducted with TIME (sessions 1-10) and GROUP (Dysphagic and Non-dysphagic) as factors with AGE as a covariate in was conducted in the Dysphagic group and Non-dysphagic group that went through SKL-I training.

There were no significant effects of within-group factors of TIME ($F(5.33, 90.62) = 1.83, p = 0.11$), TIME*GROUP ($F(5.33, 90.62) = 1.11, p = 0.36$), and TIME*AGE ($F(5.33, 90.62) = 0.51, p = 0.78$). Between-group analysis revealed that the effect of GROUP was significant ($F(1, 17) = 5.85, p = 0.03$). The effect of AGE was non-significant ($F(1, 17) = 0.001, p = 0.97$). Figure 8.1 represents the target hit-rate in each session, for the Dysphagic and Non-dysphagic groups.

There was a mean difference of 4.3% hit rate between groups (Non-dysphagic > Dysphagic, $CI [0.55, 8.13]$, Cohen's $d = 1.17$). The Non-dysphagic group had a mean hit rate of 72.1% ($CI [69.6, 74.6]$), and the Dysphagic group had a mean hit rate of 67.7% ($CI [65.2, 70.2]$).

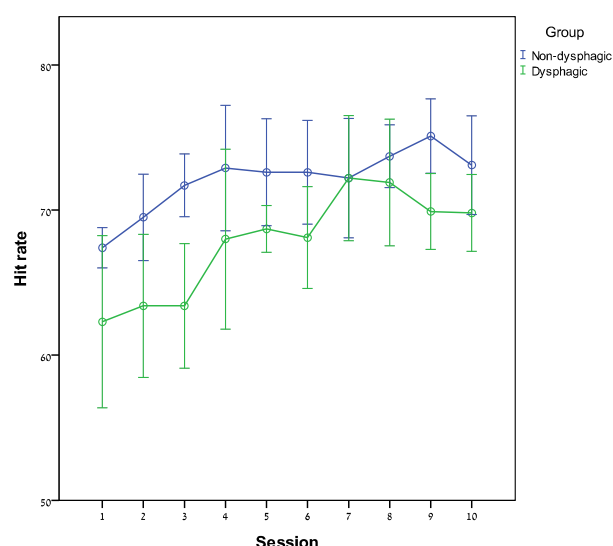


Figure 8.1 Target hit-rate (percentage) over time (session) for Dysphagic and Non-dysphagic following SKL-I training.

8.5.2.3 Summary

Over the course of training, the Dysphagic group did not increase the target hit-rate. In addition, Non-dysphagic had a significantly higher hit rate than Dysphagic, with a mean difference of 4.3%.

8.6 Discussion

This is the first study to evaluate the effects of swallowing skill training with immediate visual feedback in individuals with dysphagia secondary to PD. The key findings were that swallowing skill training resulted in increased submental activity as measured by sEMG peak amplitude in effortful swallowing tasks. In addition, there were differences in baseline measures between dysphagic and non-dysphagic subjects in submental activity in effortful swallowing tasks, but not in non-effortful swallowing tasks.

The hypothesis that there would be an increase in sEMG peak amplitude in non-effortful saliva swallowing task, and due to transference, an increase will occur in non-effortful water swallowing and in effortful swallowing tasks following SKL-I training in the dysphagic group (see 8.3.1.1) was partly supported. During effortful saliva swallowing task and during effortful 10 mL water swallowing task there was a significant and marginally significant effect of training when comparing the 1st baseline assessment to the 2nd outcome assessment. These findings indicate that cumulative effects of training took place, with an increase in submental activity following

training. In addition, these effects appeared at the 2nd outcome measure, meaning that even when the training period ended, changes still occurred. The effect sizes for the changes from 1st baseline to 2nd outcome for the effortful tasks were small. When examining the other effect sizes for these tasks, there were other small effect sizes for changes over time (e.g., increase from the 1st baseline to the 2nd baseline). Although these increases were not statistically significant, they allow for quantification of order effects that are not training-related. The non-significant change from the 1st baseline to the 2nd baseline can be explained by increased familiarity with the effortful swallowing tasks that require swallowing differently than normal. Performing these tasks twice (at the 1st and 2nd baselines) can introduce a learning effect that might influence the task performance on the 2nd baseline assessment. Hence, subtracting the effect sizes can give closer approximation to the true size of the training effect for effortful swallowing tasks, which is small. The changes from the 1st baseline to the 2nd baseline can also be attributed to variance related to the nature of the measurement tool itself. sEMG peak amplitude is influenced by many factors, including electrode positioning and subcutaneous tissue thickness that can influence proximity to the underlying muscles (Farina et al., 2004), and can also be influenced by change in head and neck position that can affect muscle length and muscle fatigue (Shinohara & Sogaard, 2006; Staudenmann et al., 2010). Surface EMG repeatability has been assessed in several studies. The repeatability of several sEMG measures from brachioradialis (forearm muscle) during sub-maximal contractions in healthy subjects was found to range between low to high (Calder, Stashuk, & McLean, 2008). Similar results were found in another study that included submaximal and maximal contraction from arm muscles (Ollivier, Portero, Maïsetti, & Hogrel, 2005). A recent study found that submental sEMG peak amplitude was consistent within and between assessment sessions in healthy subjects, when measuring saliva and 10 mL non-effortful swallowing (Huckabee, Low, & McAuliffe, 2012). Thus, in non-effortful tasks sEMG can be used to reliably assess submental activity, whereas in an effortful task there might be more variability in the measure. In addition, it is possible that sEMG measurements will have higher variability in non-healthy subject, such as individuals with PD. Hence, in the current study, the changes in peak amplitude in effortful tasks might be due to random variance.

For the non-effortful saliva swallowing task, there was a significant interaction of time and the length of dysphagia symptoms presence. Possibly, longer duration of diagnosed dysphagia might be associated with greater impairment in submental activation, although there is no evidence in the literature for this correlation in PD patients. However, disease severity has been found to be correlated with swallowing difficulties (Coates & Bakheit, 1997). Regression analysis revealed a 11.6 μ V decrease in sEMG from the 1st baseline to the 2nd outcome for each additional year in with the PD patient had observed swallowing difficulties. Furthermore, with each additional year of dysphagia, there was a 12.5 μ V decrease from the 1st baseline to the 2nd baseline. Thus, it

seems that for each additional year of having had dysphagia symptoms, the ability of the submental muscles to recover from motor exercise decreases.

Although training effects on sEMG peak amplitude were present in effortful tasks but not in non-effortful tasks, the Master's project results indicated that other changes occurred in non-effortful swallowing in this cohort. Following SKL-I training, the pre-motor and pre-swallow time shortened in non-effortful swallowing as saliva and 10 mL water, and continuous swallowing of water improved as well (Athukorala, 2012). Hence, there were improvements in swallowing execution of non-effortful (i.e., functional) swallowing tasks.

The hypothesis that the dysphagic group would demonstrate greater changes in sEMG peak amplitude following training than the non-dysphagic group (8.3.1.2) was not supported by the findings of the current study. Examination of the percent of change from baseline to outcome measures indicated that in effortful tasks, the dysphagic group had larger changes than the non-dysphagic group. This finding is supported by a study that compared changes in maximum expiratory pressure between individuals with MS and healthy controls, following EMST training (Chiara et al., 2007). Although Chiara et al. did not find significant differences between the two groups, the same trends were found, with greater changes for the group with impairments, relative to non-impaired subjects.

The hypothesis that the dysphagic group would have lower sEMG peak amplitude than the non-dysphagic group (8.3.1.2.1) was partly supported by the results. Non-dysphagic subjects had significantly higher sEMG peak amplitude in effortful swallowing tasks than the dysphagic group, with large effect sizes. This finding was not documented in previous swallowing-related literature, but it is supported by other studies that compared limb muscle strength between individuals with PD to healthy controls (Allen et al., 2009, 2010; Cano-de-la-Cuerda et al., 2010; Stevens-Lapsley et al., 2012). In a study that compared individuals with PD to healthy controls, the PD group was weaker than healthy controls when strength was measured at a maximum load task (Allen et al., 2009). Similarly, higher sEMG peak amplitude in effortful swallowing tasks is likely to translate into increased strength.

There were no differences at baseline measures between the groups in non-effortful swallowing tasks. This is surprising as dysphagia was present in the PD group, and presumably affected submental amplitude during functional swallowing. It is possible that since swallowing requires submaximal muscle activity (Burkhead et al., 2007), differences between the groups were not present in a laboratory situation due to subjects being more likely to focus strongly on the task. Thus, it is possible that if this task was conducted under muscle fatigue circumstances (e.g., eating a whole meal, eating during illness), differences between the two groups would have appeared. It

is also possible that individuals with dysphagia secondary to PD are not impaired on this measure. However, decreased muscle reserve was found in the dysphagic group in the current study by demonstrating a reduced difference between maximal and functional muscle activity in the dysphagic group in comparison to the non-dysphagic group. Hence, this finding strengthens the likelihood that laboratory findings do not necessarily reflect functional swallowing. Based on reduced muscle reserve, it can be assumed that difficulties in functional swallowing would appear under constraints like muscle fatigue or conditions that cause weakness, such as extended hospital stay (Burkhead et al., 2007). As discussed, reduced muscle reserve was also found in the older subjects (Nicosia et al., 2000; Robbins et al., 2005) and, indeed, swallowing difficulties are more prevalent with an increase in age (Shaw, 1981).

In addition, lack of differences in peak sEMG does not imply normal activation. It is possible that the functional swallowing difficulties experienced by the dysphagic group are due to reduced efficiency of motoneurons activation that will not necessarily reflect in sEMG measures. sEMG measures represent the summated electrical potential of the muscles in its vicinity (Staudenmann et al., 2010; Tassinari & Cacioppo, 2000). The same peak amplitude might be produced by different underlying mechanisms, such as the degree of coordination in recruitment and firing of motoneurons.

Integrating the results regarding baseline differences in effortful tasks, together with the results regarding percentage changes following training in effortful tasks, supports the principle of initial value in swallowing in PD. The principle states that subjects with lower initial physiological capacity will have greater capacity for improvement. Similarly, this might explain the lack of change and lack of differences in the dysphagic group in non-effortful swallowing tasks. The dysphagic and non-dysphagic groups had no differences in baseline values for those tasks as well. Thus, it is possible that the dysphagic group did not demonstrate changes, because there was no 'room' for them, since function was within normal limits at baseline.

The hypothesis regarding changes in motor performance during swallowing training in the dysphagic group (8.3.2.1) was not supported by the findings. Since the statistical model included the onset of PD and the onset of dysphagia as covariates, it might have prevented detection the training effect. Figure 8.1 presents target hit-rate over time in the non-dysphagic and dysphagic groups, and was plotted based on the raw data. Visual examination of this figure indicates that the dysphagic group had a trend towards an increase in hit rate over time. In addition, changes in submental activity were found following training, supporting the occurrence of changes in motor performance during training. It is possible that in a larger group of subjects this effect would have been detected due to increased statistical power.

The non-dysphagic group had a higher hit rate than the dysphagic group. This finding supports the proposed hypothesis (8.3.2.2). Since individuals with PD experience difficulties in movement organization due to BG deficits (Cunnington et al., 1997; Harrington & Haaland, 1991) accuracy in hitting the training target will be reduced. Cunnington et al. (1995) conducted a study that documented reduced function of the SMA during planning of a motor act of the hand in individuals with PD in comparison to healthy subjects. Since the SMA receives neural signals from the dysfunctional BG, the preparatory stage prior to motor task execution is impaired (Cunnington et al., 1995). Although during SKL-I training the target provides an external cue for the necessary amplitude and timing of swallowing, it still requires motor planning in order to achieve accuracy. A recent study describes the importance of intact neural circuit between the cortex and the BG during skill learning. Birds were trained to sing a specific complex song under two conditions: blocked and unblocked neural communication between areas equivalent to the mammalian cortex and BG. Blocking the neural communication between the two structures prevented learning, while in the unblocked condition the birds learnt the new song (Charlesworth, Warren, & Brainard, 2012). Thus, the neural impairments involved in PD affected the ability to learn the task and improve their motor performance during the task like healthy subjects.

8.7 Conclusion

This study is the first to have shown that individuals with dysphagia secondary to PD have reduced submental muscle reserve and lower submental sEMG peak amplitude in effortful swallowing tasks. Increase in submental sEMG peak amplitude in effortful swallowing tasks was found following training.

Swallowing skill training with immediate feedback using BiSSkiT software provided external visual cues (targets) for the required force and time for achieving precise swallowing execution. The rationale was that external visual cues would remove much of the need for the malfunctioning BG in the preparation and planning of swallowing, thus improving swallowing function.

Swallowing skill training with immediate visual feedback in dysphagic patients led to an increase in submental peak amplitude in effortful swallowing tasks possibly due to improvement in cortical control during effortful swallowing tasks execution. Although no changes occurred in non-effortful peak amplitude, the same cohort of subjects demonstrated improved efficiency in functional swallowing execution. It is possible that since there was no need for changes in increased submental peak amplitude in non-effortful tasks, changes did not occur. This possibility is supported by a lack of differences between dysphagic and non-dysphagic subjects in non-

effortful swallowing tasks. It is important to emphasize that this lack of difference does not necessarily mean that the individuals in the PD group did not have dysphagia. Alternatively, changes in effortful tasks occurred, in accordance with the principle of initial values that states that changes will occur if there is 'room' for those to take place and, indeed, the dysphagic group had lower submental sEMG values on the effortful task than the non-dysphagic group.

Changes in performance during training did not reach statistical significance in the dysphagic group probably due to low participant number, however the raw data suggest a trend towards an increase in hit-rate over time.

8.8 Limitations

As discussed in Sections 7.2.5 and 7.4.4, EMG amplitude was not normalized. This might have interfered with the ability to compare the EMG amplitude between and within subjects. Normalization of the sEMG data can control for the intrinsic and extrinsic variables that affect the sEMG signal (De Luce, 1997). Normalization to a reference value (which can be the maximal voluntary isometric contraction of the targeted muscle or the maximal evoked contraction) should be taken prior to measurement taking in each session for each subject. This would allow an accurate between-subject comparison.

PART IV: BASELINE

DIFFERENCES IN MEP

CHARACTERISTICS

CHAPTER 9: BASELINE

DIFFERENCES IN SUBMENTAL MEPS

CHARACTERISTICS

9.1 Introduction

Brain plasticity can be defined as “nature's invention to overcome limitations of the genome and adapt to the rapidly changing environment” (Pascual-Leone et al., 2005), with plastic changes occurring throughout the life span (Pascual-Leone et al., 2011). It has been suggested that plastic changes in the elderly reflect a compensatory mechanism that consists of a generalized, non-specific use of neural resources to accommodate behaviour in response to a perceived increase in demand (Pascual-Leone et al., 2011; Zöllig & Eschen, 2009). This might be the case for swallowing as well.

Rehabilitation of neurological dysphagia aims to capitalize on the capacity for plastic changes. In recognition of potential neural adaptation, studies of rehabilitation techniques have recently focused on documenting not only peripheral biomechanical changes but also change in underlying neural function (Ward et al., 2003). The broader scope of this thesis was to document changes following swallowing training in healthy adults, including measurements of neural adaptation. However, investigation of neural excitability assessed at baseline in the different age groups was imperative for interpretation of results.

9.2 Literature review

9.2.1 Age effects on brain activation during motor tasks

Zöllig & Eschen (2009) discussed neural plasticity associated with cognitive changes in the elderly, but the principles they raised are relevant for understanding age-related differences seen in neural activation during motor tasks. Although some studies reported a similar level of performance on cognitive tasks, the neural activation patterns were different, with the older subjects having increased activation (Cabeza, 2002; Reuter-Lorenz et al., 2000). This type of finding can be explained in terms of a *compensatory* mechanism by which neural activity must be

increased in order to attain the same performance of younger subjects. However, increased neural activation in older subjects was also detected in the presence of inferior performance when compared to younger subjects (Colcombe, Kramer, Erickson, & Scalf, 2005; Zarahn, Rakitin, Abela, Flynn, & Stern, 2007). This finding, in turn, may indicate an *inefficient* neural activation mechanism, whereby the increased activation was not sufficient to generate the desired outcome (i.e., similar to that of the younger subjects' performance) (Zöllig & Eschen, 2009).

Specific to motor performance, some papers support a *compensatory* role of increased activation, where the increased activation accompanies a motor output similar to that of younger subjects. Mattay et al. (2002) reported that older subjects with a similar accuracy level and similar reaction times to those of younger subjects had greater brain activation in the contralateral sensorimotor cortex, lateral premotor area, supplementary motor area, and ipsilateral cerebellum. These areas were activated in young subjects as well, but to a lesser extent. Activation was also present in additional areas that were not activated in younger subjects, such as the ipsilateral sensorimotor cortex, putamen, and contralateral cerebellum. In contrast, older subjects who had longer reaction time on the same task (i.e., reduced performance), also had reduced neural activation in the primary motor cortex (bilaterally), the premotor cortex, SMA, cerebellum, and the contralateral parietal cortex. Thus, it is possible that in order to achieve performance level that matches that of younger subjects, over-activation of brain areas that participate in movement performance, and recruitment of additional areas are essential (Mattay et al., 2002; Ward, 2006). Similar findings were reported in an fMRI study that compared two different motor tasks performed by the dominant and the non-dominant hand (Hutchinson, 2002). Although similar performance levels were present, the results indicated that with increased level of difficulty (using the non-dominant hand and performing the more difficult motor task) the differences between the two age groups in neural activation patterns became larger, with more activation in bilateral SMA and ipsilateral sensorimotor cortex in the older subjects (Hutchinson, 2002). Since motor output was similar between the two age groups, the increased activation pattern was explained in terms of a compensatory mechanism.

Reduction in neural activation was associated with reduced motor performance (Mattay et al., 2002), as supported by an fMRI study that documented longer reaction times when performing a simple motor task in older subjects, when compared to younger subjects. This finding was accompanied by a reduction in the number of activated voxels in the central sulcus in older subjects, in comparison to younger subjects (D'Esposito, Zarahn, Aguirre, & Rypma, 1999).

In contrast, other studies have found that increased neural activation was associated with reduced motor performance. Older subjects had diffuse areas of activation that were related to longer reaction time during performance of a motor task (Langan et al., 2010; Riecker et al., 2006).

These two fMRI studies (Langan et al., 2010; Riecker et al., 2006) found diffuse, bilateral, non-specific, neural activity in the older subjects, which was greater in the ipsilateral hemisphere. For example, when activating the right finger, activation was present in the left sensorimotor cortex in both age groups, but older subjects had shown activation also in the ipsilateral (right) sensorimotor cortex, and ipsilateral premotor cortex (Riecker et al., 2006). In areas that were more specifically related to the motor activity performed, like the left pre-SMA and left sensorimotor cortex, younger subjects had greater activation than older subjects (Riecker et al., 2006). Langan et al. (2010) found a strong positive correlation ($r = 0.57$) in older subjects, according to which those who had longer reaction times also had greater activation in the ipsilateral sensorimotor cortex. It is, thus, possible that for limb movements, over-activation (in terms of ipsilateral M1 activation) would negatively interfere with the performance of unilateral limb movement. Alternatively, it is also possible that activation of the ipsilateral hemisphere in older subjects facilitates motor performance, and presumably without over-activation, motor performance would have been worse.

When interpreting age-related differences from fMRI studies, it is important to take into account potential confounds that may influence the BOLD signal, like the presence of baseline differences in signal-to-noise ratio of the neural activity. Older subjects have reduced signal-to-noise ratio which might mask the presence of task-related BOLD changes (D'Esposito et al., 1999; Ward, 2006). Reduction in neurovascular coupling can result in reduced signal-change due to inefficient vascular response to the increased neural activation. However, it is hard to distinguish this possibility from an alternative option of adequate vascular response to decreased neural activation, since both would result in reduced change in the BOLD signal.

9.2.2 Age effects on MEPs in non-swallowing motor tasks

TMS studies also produce contradictory results regarding the effect of age on the magnitude of MEP measured from different hand muscles. A positive correlation between MEPs amplitude and age was reported for hand movement task (Bernard & Seidler, 2012). Increased magnitude with an increase in age could be explained in terms of increased cortical excitability, given a lower motor threshold in older subjects. Increased MEP magnitude can also be explain in terms of recruitment of larger motor units in older subjects (Bernard & Seidler, 2012; Fling, Knight, & Kamen, 2009). With an increase in age, the number of motoneurons decreases (Johnson & Duberley, 1998). Thus, a reduction in muscle fibres occurs as well, since the fibres go through denervation process due to the loss of motoneurons, which leads to muscle atrophy (Faulkner et al., 2007). The first type of motor neurons that are lost are the larger motor units (Mittal & Logmani, 1987) which are, according to the size principle, recruited at high force demands

(Gordon, Thomas, Munson, & Stein, 2004). The remaining muscle fibres are of small and medium sizes, and are slow-twitching (Lexell, 1995). Some of these go through a remodeling process in which they are re-innervated by other motoneurons, leading to large sized motor units of slow-twitching fibres (Fling et al., 2009). This can be the cause of the larger MEP amplitude detected in the elderly. Increased MEP magnitude might also be explained in terms of decreased excitability of intracortical inhibitory neurons that results in reduced inhibition of the neural activity, and in enhanced neural activation. This explanation is supported by a study that employed a paired-pulse inhibition protocol in which subthreshold TMS stimulation is given 1- 5 ms prior to a suprathreshold stimulation. The results demonstrated a reduced inhibitory effect in older subjects in comparison to younger subjects (Peinemann et al., 2001). Interestingly, McGregor et al. (2011) and Peinemann et al. (2001) found reduced inhibition in older adults in comparison to younger subjects, but in other studies (Cirillo et al., 2011; Rogasch et al., 2009) no difference was found. This difference might be related to different methodology. McGregor et al. measured the length of the silent period following the MEP as a marker for inhibition, but others (Cirillo et al., 2011; Rogasch et al., 2009) used a paired-pulse paradigm in which two magnetic pulses were delivered to the contralateral hemisphere to the active hand. However, Peinemann et al. also used the same technique of paired-pulse stimulation but did find reduced neural inhibition in older subjects. Looking closely at the data provided in both the Cirillo et al. and Rogasch et al. papers, both reported on *p*-values of 0.10 when examining age-related difference in inhibition, with older subjects having a trend towards reduced inhibition in comparison with younger subjects. Hence, it is possible that with a larger sample size, a difference would have been detected in their studies as well.

Other researchers reported an opposite trend, with lower MEP magnitudes in older subjects (Fujiyama, Garry, Levin, Swinnen, & Summers, 2009; Oliviero et al., 2006). Reduced magnitude of MEP can be the result of reduced synchronization of I-waves (Oliviero et al., 2006), decreased amount of motoneurons recruited, or due to recruitment of the same amount of motoneurons in a less synchronized fashion, resulting in phase cancellation as registered by sEMG electrode placed at the end organ (Oliviero et al., 2006; Pitcher, Ogston, & Miles, 2002). Reduced MEP magnitude can be also due to decline of the neuromuscular system resulting in impaired physical function, and decreased muscle mass and strength (Berger & Doherty, 2010). In addition, some researchers found an increase of the motor threshold with age, meaning that elicitation of an MEP required a higher degree of magnetic stimulation, which possibly indicates decreased cortical excitability with age (Matsunaga, Uozumi, Tsuji, & Murai, 1998; Rossini, Desiato, & Caramia, 1992).

Some studies reported no significant age effects of baseline MEP magnitude (Fathi et al., 2010; Tecchio et al., 2008), however these studies measured rest MEPs. Age-related differences in MEP related to movement might only exist once a motor task is introduced.

9.2.3 Correlation between MEPs and BOLD signal

TMS and fMRI are frequently used to assess brain activation during motor performance in healthy subjects. Although, these tools measure different processes, several studies found that the output of these two methods complemented each other, and similarly reflected the spatial organization of the motor cortex (Foltys et al., 2000; Rossini et al., 1998). The focal activity in M1 detected using fMRI has been shown to be almost identical to TMS maps of M1 (Boroojerdi et al., 1999; Krings et al., 1997; Lotze et al., 2003; Niyazov, Butler, Kadah, Epstein, & Hu, 2005), with only 4-22 mm mismatch between the two measurement tools (Niyazov et al., 2005). In addition, the area from which the peak of the MEP response and peak of the BOLD response were recorded are also very similar (Boroojerdi et al., 1999).

However, these findings were not replicated in non-healthy participants. Foltys (2003) found that in stroke patients there was no correlation between the extent of activation seen in fMRI and the motor output maps found with TMS. Ten stroke patients who experienced a unilateral paresis and had a rapid motor recovery were examined. The fMRI study revealed no differences between M1 activity in the affected and non-affected sides, while TMS revealed smaller MEP magnitude in the affected side versus the non-affected, indicating the presence of impairment in neural output of the affected hemisphere (Foltys, 2003). This difference between the fMRI and TMS findings was explained by differences in the characteristics of the two tools, with fMRI reflects the intracortical processing in M1 whereas TMS provides information regarding the output of M1 as measured at the level of the associated muscles (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001). A positive correlation was found between the MEP threshold and the motor impairment, with a higher threshold found in post-stroke patients who had more impairments (Foltys, 2003). Other studies provided support to the correlation between motor impairments and TMS measures (Byrnes, Thickbroom, Phillips, & Mastaglia, 2001; Cicinelli, Traversa, & Rossini, 1997; Traversa et al., 2000), with lower MEP amplitude associated with decreased motor function (Koski, Mernar, & Dobkin, 2004; Piron, Piccione, Tonin, & Dam, 2005).

9.2.4 Age-related differences in brain activation during swallowing

Martin et al. (2007) were the first to measure swallowing-related brain activation in older female participants (nine females, mean age \pm SD: 74 ± 8 yr). They evaluated saliva and 3 mL water swallowing tasks and found substantially greater brain activation within the sensorimotor, premotor and prefrontal cortices during the water task in comparison to the saliva task. This difference between the tasks was attributed to task difficulty with a need to hold the water in the oral cavity while lying supine, which requires more control over the bolus to avoid penetration or aspiration. In this study Martin et al. did not directly compare age groups (Martin et al., 2007).

Later, Humbert et al. (2009) performed a direct comparison between younger ($n = 12$, mean age \pm SD: 28 ± 4 yr) and older ($n = 11$, 72 ± 7 yr) subjects during saliva, water and barium swallowing tasks using fMRI. They documented greater BOLD responses in several areas, including the primary motor cortex (i.e., BA4 or M1) in older participants compared to younger subjects. Increased activation in the older subjects might serve as a compensatory mechanism to offset what would otherwise be decreased swallowing function with age (Robbins et al., 1992) including increased swallowing duration, decreased tongue pressure (Robbins et al., 1995), delayed pharyngeal swallowing (Logemann, 1990; Robbins et al., 1992), and increased prevalence of aspiration (Butler et al., 2011). The exact reason for changes in swallowing function is not clear. Diminished muscle mass and reduced strength above the age of 60 (Evans, 1995) has been suggested as a possible cause. Increased activation might indicate increased excitability and a more diffuse, less specific, neural response during swallowing in order to perform the swallowing motor task. If indeed the increased activation in older subjects is related to changes in swallowing function in comparison to younger subjects, then the over-activation can be explained in terms of a compensatory mechanism, provided that the outcome is the same. This is similar to findings from the limb movement literature (see Section 9.2.2), that has demonstrated an association between increased brain activation with similar performance level in older subjects (Mattay et al., 2002).

In contrast to Humbert et al. (2009), a recent study compared the BOLD responses between younger ($n = 10$, 22 ± 2 yr) and older ($n = 9$, 70 ± 4 yr) subjects and found that during a water swallowing task, the younger group had greater neural activation in primary sensory areas, and also in the posterior BA4 (Malandraki et al., 2011). Decreased activation in older subjects could account for a decline in swallowing biomechanics associated with age (Humbert & Robbins, 2008; Robbins et al., 1995), similar to the findings from the limb literature, with over-activation of additional brain areas correlated with decreased motor performance (Langan et al., 2010). The

discrepancy between the results of Humbert et al. (2009) and Malandraki et al. (2011) might be explained in terms of methodological differences between the two studies with a different in bolus size. Differences in the statistical analysis might also explain the differences in results, with mixed effect model used by Malandraki et al. (2011), where subjects were treated as random effects, and fixed-effects model used by Humbert et al. (2009). Random-effects modelling of fMRI data was suggested to have an advantage over a fixed-effects model in interpreting age-related differences, since the variation in signal-to-noise ratio is taken into account by the model (D'Esposito et al., 1999; Ward, 2006). As mentioned before, it has been reported that with an increase in age, the neural signal-to-noise ratio decreases. This decrease introduces difficulties in detecting suprathreshold activated voxels, due to the already noisy neural activity background in the older subjects. Thus, a lower ratio exists between the changes in the signal associated with the activity and the residual variance (D'Esposito et al., 1999).

9.2.5 Exploring M1 function in swallowing

Swallowing-related MEPs induced by TMS over M1 are commonly used to measure changes following intervention. M1 has been the focus of investigation in several studies on swallowing recovery following stroke (Hamdy, Aziz, Rothwell, Crone, et al., 1997; Hamdy, Aziz, et al., 1998), and has been used to document neural changes following swallowing-related training (Boudreau et al., 2007; Macrae, 2011; Svensson et al., 2003, 2006).

M1 has been suggested to have a role in initiating the swallowing sequence, and in modulating and priming the pharyngoesophageal component of swallowing (Ertekin & Aydogdu, 2003; Fraser et al., 2002; Hamdy, Mikulis, et al., 1999; Kern, Jaradeh, et al., 2001; Martin et al., 2004, 2001; Mosier & Bereznaya, 2001; Mosier, Liu, et al., 1999; Suzuki et al., 2003). M1 has also been identified as having the capacity of coding complex movement sequences and can be the area in which long-term representation of acquired motor skills takes place (Karni et al., 1998). Some research work has demonstrated that swallowing-related practice can affect M1. Svensson et al. (2003; 2006) documented plastic changes in M1 following one hour of tongue-protrusion training (Svensson et al., 2006) as well as 7 days of training (Svensson et al., 2003). They concluded that M1 is adaptive and dynamic in response to new motor tasks, and may contribute to learning complex tasks, such as bolus preparation during the oral stage.

Age-related differences in submental MEPs recorded during swallowing have not been investigated. Such differences may clarify the role of M1 in swallowing and may also have ramifications for measuring neural changes following swallowing rehabilitation by taking into consideration possible age-related differences.

9.3 Aim

This study was not hypothesis-driven, but rather an example of “discovery science” (Glass, 2010; Nussenblatt, Marincola, & Schechter, 2010) as results were discovered through exploration of the existing data. The aim of this further exploration was to identify baseline differences in MEP measures that could affect the interpretation of the main study’s findings.

9.4 Methods

9.4.1 Participants

Forty healthy participants (20 males, 20 females; 20 young, 20 old) were recruited as part of the main study (for details regarding recruitment process, exclusion criteria and ages see Section 5.1.1).

MEPs were elicited in 30 of the 40 participants during contraction and in 29/40 during swallowing. The inability to elicit swallowing-MEPs and contraction-MEPs from the submental area has been previously reported (Abdul Wahab et al., 2010; Doeltgen et al., 2010), and might be related to the coil’s position and angle in relation to M1 or the distance between the coil and the motor cortex (see Section 2.1.1 – *Swallowing related MEPs*). One subject was excluded since her MEP magnitude was larger than three *SD* from her age-group mean. The age, standard deviation, and age range of the subjects who had MEPs in volitional contraction ($n = 30$) in each age group are presented in Table 9.1.

Table 9.1 Subjects with MEPs during volitional contraction ($n = 30$): Age in years \pm *SD* (range) in each age group, by gender in each age group and by age group in total

Age group	Gender	Age by Gender	Age by Age Group
Young ($n = 16$)	Female ($n = 10$)	25.6 ± 5.1 (21-35)	25.5 ± 4.4 (21-35)
	Male ($n = 6$)	25.5 ± 3.7 (21-30)	
Old ($n = 14$)	Female ($n = 6$)	65.2 ± 8.7 (53-77)	67.1 ± 9.9 (53-85)
	Male ($n = 8$)	68.5 ± 11.1 (54-85)	

9.4.2 Instrumentation

For details, see Section 5.2.1 – *MEP instrumentation*.

9.4.3 Procedure

The procedure for MEP collection was composed of a single baseline session in which the excitability of the corticobulbar projections to the submental muscle group was assessed using single-pulse TMS over the submental-related hotspot during two tasks: volitional saliva swallowing and volitional submental muscle contraction. The MEP was registered from sEMG electrodes located over the submental muscle group at midline. Details regarding the procedure for MEPs collection were reported in Section 5.4.4 – *MEP procedure*.

9.4.4 Data extraction

Details regarding data extraction were reported in Section 5.7.1 – *MEP data*.

9.4.5 Statistical analysis

Statistical analyses were conducted using SPSS statistics package (IBM SPSS Statistics version 19.0). To evaluate for differences in MEP magnitude between younger and older subjects in volitional contraction and volitional swallowing, a t-test for unpaired samples was used to examine age effects. In addition, MEP latency was tested for differences between age groups for both tasks using unpaired t-test. Differences in MEP size and magnitude were also analyzed to test for gender effects using t-tests for unpaired samples. In addition, differences between the two tasks were tested using a t-test for unpaired samples. Significance value was set at $\alpha \leq 0.05$. Marginally significant results were defined as $0.05 < \alpha \leq 0.10$. All tests were two-sided. Correction for multiple comparisons was not applied due the exploratory nature of this study (Nakagawa, 2004; Phillips, 2004; Robey, 2004a). Confidence intervals (*CI*) are reported as 95% *CI* around the mean difference or around the mean, and will appear in the text as *CI*.

9.5 Results

9.5.1 Differences between younger and older subjects in MEP magnitude

Volitional submental contraction

Leven's test for equal variance was significant ($p < 0.05$) meaning that the two samples had unequal variance, thus Welch's t-test for unequal variance for unpaired samples was conducted. The results revealed that the older group had larger MEP magnitude ($n = 14$, $M = 2614 \mu V \cdot ms$, $SD = 1239$) than the younger group ($n = 15$, $M = 1769 \mu V \cdot ms$, $SD = 724$) during volitional

contraction ($t(20.65) = 2.22, p = 0.03, CI$ of the mean difference $[-53, -1636], d = 0.87, R^2$ (Adj.) $= 0.13$) (Figure 9.1).

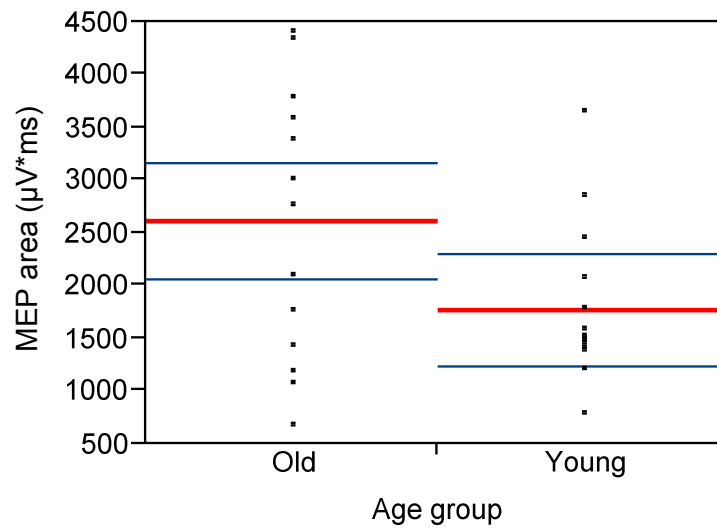


Figure 9.1 Age differences in MEP area ($\mu V*ms$) recorded during volitional contraction. The red line represents the mean and the blue lines represent 95% confidence intervals

Volitional saliva swallowing

Again, Leven's test for equal variance was significant ($p < 0.05$), thus Welch's t-test was employed. The results revealed that the older group ($n = 14$) had larger MEP magnitude ($M = 2891 \mu V*ms, SD = 1229$) than the younger group ($n = 14, M = 1926 \mu V*ms, SD = 645$) during volitional saliva swallowing ($t(19.65) = 2.6, p = 0.01, CI$ of the mean difference $[-190, -1740], d = 1.02, R^2 = 0.17$) (Figure 9.2).

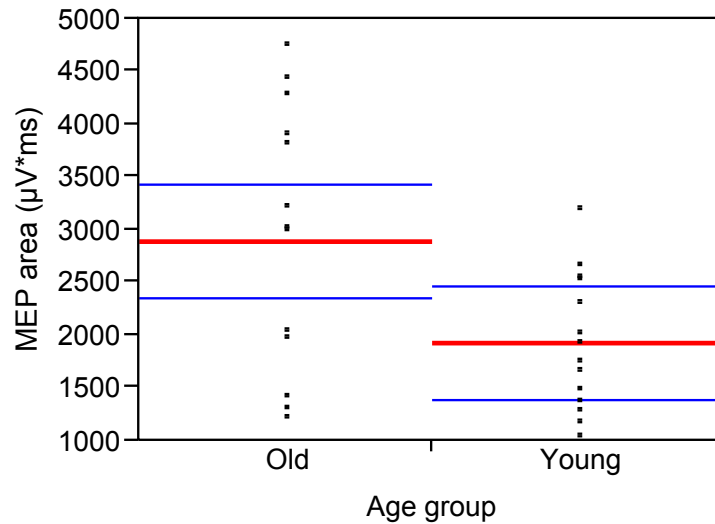


Figure 9.2 Age differences in MEP area ($\mu V \cdot ms$) recorded during volitional saliva swallowing. The red line represents the mean and the blue lines represent 95% confidence intervals

9.5.2 The relationship between age and MEP magnitude

Since a difference was found between the two age groups, an additional analysis was conducted in order to answer an additional question: can a regression analysis rather than a categorical (Old vs. Young) comparison be used to examine age-related effects on MEP magnitude in a continuous fashion? A simple linear regression line was fit to the data as a secondary investigation, taking into account that data was missing for the age group between 36 to 52 years of age.

Volitional submental contraction

Age significantly predicted MEP magnitude ($F(1, 27) = 5.69$, $p = 0.02$, R^2 (Adj.) = 0.14, $B = 19.88$, CI for B [2.79, 36.97], standardized beta (β) = 0.41). With every year increase in age, the MEP area increased by 19.9 $\mu V \cdot ms$ (Figure 9.3).

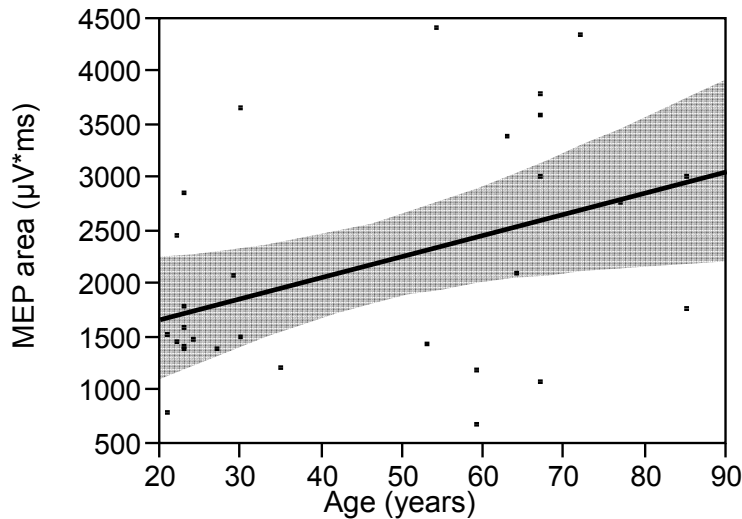


Figure 9.3 Linear regression: the effects of age (in years) on MEP area ($\mu V \cdot ms$) during volitional contraction. The black line represents the linear fit and the shaded grey areas around it represent 95% confidence intervals around the linear line.

Volitional saliva swallowing

Age significantly predicted MEP magnitude ($F(1, 26) = 10.15, p = 0.003, R^2 = 0.25, B = 25.19, CI$ for B [8.94, 41.44], standardized beta (β) = 0.53). With every year of increasing age, the MEP area increased by 25.2 $\mu V \cdot ms$ (Figure 9.4).

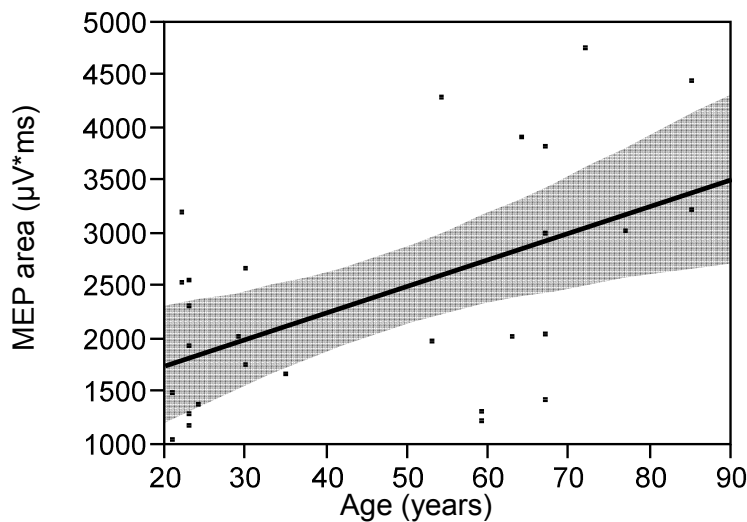


Figure 9.4 Linear regression: the effects of age (in years) on MEP area ($\mu V \cdot ms$) during volitional swallowing. The black line represents the linear fit and the shaded grey areas around it represent 95% confidence intervals around the linear line.

9.5.3 Differences between younger and older subjects in MEP latency

Volitional submental contraction

There was no significant difference in onset latency between the older group ($n = 14$, $M = 8.96$ ms, $SD = 2.09$, CI for the mean $[7.75, 10.17]$) and the younger group ($n = 15$, $M = 8.31$ ms, $SD = 1.83$, CI for the mean $[7.29, 9.33]$) during volitional contraction ($t(27) = 0.89$, $p = 0.37$, CI of the mean difference $[-0.85, 2.15]$, $d = 0.00$, R^2 (Adj) = 0.01).

Volitional saliva swallowing

No significant difference was found in onset latency between the older group ($n = 14$, $M = 8.76$ ms, $SD = 1.97$, CI for the mean $[7.62, 9.89]$) and the younger group ($n = 14$, $M = 8.25$ ms, $SD = 1.59$, CI for the mean $[7.33, 9.18]$) during volitional swallowing ($t(26) = 0.73$, $p = 0.46$ (2-sided), CI of the mean difference $[-0.89, 1.89]$, $d = 0.30$, R^2 (Adj) = 0.02).

9.5.4 Differences between genders in MEP magnitude

Volitional submental contraction

There was no significant difference MEP area between males ($n = 14$, $M = 2133$, $SD = 1028$, CI for the mean $[1540, 2727]$) and females ($n = 15$, $M = 2217$, $SD = 1155$, CI for the mean $[1577, 2857]$) during volitional contraction ($t(27) = 0.20$, $p = 0.83$, CI of the mean difference $[-752, 919]$, $d = 0.08$, R^2 (Adj) = 0.03).

Volitional saliva swallowing

No significant difference was found in MEP area between males ($n = 13$, $M = 2533$ ms, $SD = 1214.6$, CI for the mean $[1799, 3267]$) and females ($n = 15$, $M = 2300$, $SD = 981$, CI for the mean $[1757, 2843]$) during volitional swallowing ($t(26) = 0.56$, $p = 0.57$, CI of the mean difference $[-620, 1086]$, $d = 0.22$, R^2 (Adj) = 0.02).

9.5.5 Differences between genders in MEP latency

Volitional submental contraction

There was no significant difference in onset latency between males ($n = 14$, $M = 8.20$ ms, $SD = 2.02$, CI for the mean $[7.03, 9.38]$) and females ($n = 15$, $M = 9.02$ ms, $SD = 1.87$, CI for the mean

[7.98, 10.05]) during volitional contraction ($t(27) = 1.12$, $p = 0.27$, CI of the mean difference [-0.67, 2.29], $d = 0.44$, R^2 (Adj) = 0.01).

Volitional saliva swallowing

No significant difference was found in onset latency between males ($n = 13$, $M = 8.06$ ms, $SD = 1.24$, CI for the mean [7.31, 8.81]) and females ($n = 15$, $M = 8.89$ ms, $SD = 2.11$, CI for the mean [7.72, 10.06]) during volitional swallowing ($t(26) = 1.24$, $p = 0.22$, CI of the mean difference [-0.53, 2.20], $d = 0.49$, R^2 (Adj) = 0.02).

9.5.6 Task effects on MEP magnitude

A t-test for unpaired samples revealed no significant difference in MEP area between volitional swallowing ($n = 28$, $M = 2408.5$, $SD = 1080.9$, CI for the mean [1989, 2828]) and volitional contraction tasks ($n = 29$, $M = 2177$, $SD = 1077$, CI [1767, 2586]) ($t(55) = 0.81$, $p = 0.42$, CI for the mean difference [-341, 805]).

9.5.7 TMS output and hotspot side by age group

The hotspot and the TMS output were determined individually, as reported in Section 5.4.4. Since there were differences between age groups, two additional analyses were conducted to measure if the TMS output used to record the MEPs was different between age groups and if the side of the hotspot (right or left) was different between age groups.

A t-test for two unpaired samples revealed no significant difference in TMS output between older subjects ($n = 14$, $\bar{x} = 52.1$, $SD = 1.6$, CI for the mean [48.8, 55.5]) and younger subjects ($n = 16$, $\bar{x} = 54.1$ ms, $SD = 1.5$, CI for the mean [50.9, 57.2]), ($t(28) = 0.88$, $p = 0.38$, CI of the mean difference [-2.6, 6.5], R^2 (Adj) = 0.00).

Fisher's exact test revealed no significant differences ($p = 1.00$) in the side of the hotspot between older subjects ($n = 14$, 7 left, 7 right) and younger subjects ($n = 16$, 9 left, 7 right).

9.6 Summary of results

There were significant differences between older and younger subjects in MEP magnitude during volitional saliva swallowing and volitional submental contraction, with older subjects having a larger MEP area than younger subjects. A regression model was used to assess the relationships between MEP magnitude and age. With every year of increased age, contraction MEP area

increased by 20 $\mu\text{V}\cdot\text{ms}$, and swallowing MEP area increased by 25 $\mu\text{V}\cdot\text{ms}$. Age had no effect on MEP latency in both tasks. Gender had no effect on MEP magnitude or latency in both tasks. There were no differences in MEP magnitude between the two tasks. Lastly, TMS output was not different between the two age groups, nor was a difference in the dominant hemisphere for TMS.

9.7 Discussion

This study investigated the effects of age on submental MEPs (magnitude and latency) during volitional swallowing of saliva, which reflects a functional swallowing task, and contraction of the submental muscles, which reflects a non-functional task. In addition, gender effects on MEPs and task-related difference in MEPs were tested. The aim was to identify differences that could be integrated with the main study findings (Part I) while interpreting its results.

The finding of increased MEP magnitude in the older subjects may reflect an increase in efferent cortical drive during the execution of volitional saliva swallowing and volitional submental contraction tasks with advanced age. The current results are supported by Humbert et al.'s (2009) fMRI study that documented increased activation during different swallowing tasks including saliva swallowing. They are also consistent with a study that measured MEP from the hand muscles and found greater MEP magnitude in the older group in comparison to the young group (Bernard & Seidler, 2012). However, the results of the current study are not supported by Malandraki et al. (2011) findings that reported on the opposite trend, with increased neural activation in the younger group in comparison to the older group.

The age differences in cortical drive may reflect increased muscular or biomechanical effort in executing both tasks (saliva swallowing and submental contraction) in the older subjects (Humbert et al., 2009; Kelly et al., 2006) in comparison to younger subjects. Integration of biomechanical measures with neural measures can produce important information regarding the possibility of positive relationship between larger MEP and increased effort.

Increased neural excitation can also be attributed to diminished excitation of inhibitory interneurons as found by (Peinemann et al., 2001). This mechanism was not explored in swallowing.

Although no significant difference in TMS output was found between the two age groups, this does not indicate that the same level of excitability exists for both age groups. The TMS output chosen for each subject was the level at which a consistent MEP was recorded, characterized by an amplitude that was half the size of the maximal MEP recorded during volitional contraction. Threshold testing for submental MEPs was not conducted in the present study, but had submental

MEPs threshold testing been recorded and differences were found between the age groups during muscle rest, with older subjects having lower threshold than younger subjects, this would support the suggestion of increased excitation in the older group (Matsunaga et al., 1998; Rossini et al., 1992). On the other hand, if a similar threshold had been found for the two age groups, then the difference between the age groups could be explained in terms of differences in motor unit recruitment patterns, with older people recruiting larger motor units than young (Bernard & Seidler, 2012; Fling et al., 2009).

As mentioned previously, swallowing function changes with age (Robbins et al., 1992), although the reason for this is not clear. Some suggest that a reduction in muscle mass, diminished strength, and loss of motor units with age – known as sarcopenia (Evans, 1995) – is the underlying physiological basis. Age-related changes in submental musculature have not been reported in the literature. However, reduction of the muscle thickness of the tongue has been reported (Tamura, Kikutani, Tohara, Yoshida, & Yaegaki, 2012), together with a reduction in muscle reserve (Nicosia et al., 2000; Robbins et al., 2005). In addition, laryngeal muscles in the rat change to slower-contracting motor units with increase in age (Suzuki et al., 2002). In humans, age-related changes in pharyngeal muscle composition have also been documented, along with decline in endurance (van Lunteren, Vafaie, & Salomone, 1995). Thus, it is possible that there are age-related changes in submental structure or innervation properties, which might affect MEP magnitude. The submental muscle group might also be influenced from age-related changes, including the loss of larger motoneurons leading to atrophy (Johnson & Duberley, 1998; Mittal & Logmani, 1987), re-innervation of muscle fibres by neighbouring motoneurons, and creation of motor units that consist of a large number of slow twitching muscle fibres (Fling et al., 2009).

Age-related changes in swallowing biomechanics may also be attributed to changes in cortical activation. In a study that included a task that required isolated activation of the fingers, older subjects had decreased selectivity in neural downflow in comparison to younger subjects, as manifested by M1 facilitation of other muscles unrelated to the task (Léonard & Tremblay, 2007). Since swallowing requires precise execution of the motor event, recruitment of additional brain areas might impede swallowing.

The current study reveals for the first time that older subjects have increased submental MEP magnitude in comparison to young subjects. The results can support both hypotheses for decreased swallowing function with age - a biomechanical/muscular reason and neurological reason. It is possible that older subjects had increased MEPs due to central or peripheral changes.

Age did not influence MEP latency. This finding is partly supported by a study that investigated the effect of age on MEPs from the upper limb (Bernard & Seidler, 2012). There were no effects

of age when measuring the latency of the ipsilateral hand, however there was a trend towards longer latencies in older subjects when the contralateral hand was measured (Bernard & Seidler, 2012). In addition, no differences between age groups were found in MEP amplitude in the ipsilateral side, while in the contralateral side the older group had larger MEPs. The relationship between longer latency and larger MEPs in older subjects might be due to the changes in motor unit composition with age. The fast-twitch motor units decrease in number and the slow-twitch motor units increase (Fling et al., 2009; Lexell, 1995). While performing a motor task, larger groups of slow-twitching muscle fibres are recruited since the fast-twitch units are lost. This alternation with age was suggested as a possible explanation for larger MEP amplitude (Bernard & Seidler, 2012), but might also explain the increased latency in older subjects. In the current study, there was a trend for older subjects to have a slightly longer latency than younger subjects (non-significant difference). Thus, it is possible that age-related differences in submental MEPs latency do exist but due to the small sample size they were not detected.

No significant differences in submental MEP amplitude were found between the two volitional tasks of submental muscles contraction and swallowing. The lack of a difference is contradicted by a study that compared the magnitude of the MEP response in young subjects, and found that swallowing-related MEPs were smaller than contraction-related MEPs (Doeltgen et al., 2011). The discrepancy in results might be due to the difference in the instructions giving to the subjects for the volitional swallowing task. In the current study, the instruction was “Swallow your saliva; try to swallow with no effort, as you usually swallow”, while in Doeltgen et al. (2011), the instruction was to swallow saliva while limiting volitional oral movements and keeping the tongue as relaxed as possible (p. 89). The instructions for volitional contractions were the same in both studies (“Contract the muscles under your chin as if you were trying to stifle a yawn”), however Doeltgen et al. (2011) added to it the instruction to restrict tongue movements. Since tongue movement is important for swallowing initiation (Miller, 2008), asking to restrict its movement might have created an alternation in swallowing. This might have led to decreased muscle activation. Hence, in the Doeltgen et al. (2010) study a difference was found between the two conditions, since restricting the tongue movement during the contraction task might have a lesser degree of influence on muscles activation in comparison to its effect on swallowing, in which tongue restriction might lead to decreased muscle activation.

Gender did not influence the magnitude and the latency of the MEP. This finding is supported by a study that documented no gender effects on MEP response characteristics including its magnitude in younger and older subjects. Latency was not measured in that study (Pitcher et al., 2002). Another study measured MEPs from the upper limb and found no gender effects on MEP magnitude and latency in younger subjects, after correcting the latencies for the subject's arm

length (Livingston, Goodkin, & Ingersoll, 2010). It is possible that the studies that reported on gender effects on MEPs found those differences since they did not adjust the latency to the limb's length (Tobimatsu, Sun, Fukui, & Kato, 1998). When assessing corticobulbar excitability from the submental muscles in females and males, no differences in latency exist.

9.8 Conclusions

The study documented increase in swallowing-related MEP magnitude in older subjects. This finding might be related to reports regarding changes in swallowing function with age, although further research is needed to clarify this possibility. Increased MEP can be the result of peripheral or central age-related changes, including changes to the properties of the motor units or changes to neural inhibition levels. Changes to swallowing function with age are usually explained in terms of changes to the periphery (weakness, hypotrophy), however this study suggests that central changes could also be the reason.

The data suggest that increased M1 activation might accommodate and 'protect' the swallowing function from deterioration, as the older subjects in the study reported on no swallowing difficulties. Thus, M1 role in swallowing might be in sending neural signal to allow motor activation but with increased age, there might be reduced inhibitory control circuits that regulate M1 activity, thereby serving as a compensatory mechanism. Thus, the role of M1 in swallowing might be in adjusting swallowing function by increasing the downflow to the targeted muscles.

In addition, age did not have an effect on MEP latency, and gender did not affect MEP magnitude or latency. There were no differences in MEP magnitude between the two tasks. Data from the current study emphasize the importance of using different reference points for evaluation of MEPs for each age group.

9.9 Limitations

The current study did not employ any MEP normalization technique. This might have interfered with the ability to compare MEPs between subjects. As discussed in Section 7.2.5 since MEPs were measured using sEMG electrodes, their magnitude is influenced by many factors, which can vary between individuals and thus influence the ability to conduct between-subjects comparison. These factors include technical, anatomical and physiological factors such as the location of the electrodes along the muscle, their proximity to the innervation points of the muscles by the motoneurons, the thickness of the fatty tissue, the blood flow in the muscle, and fibre type composition, all of which differ between subjects (De Luca, 1997). Thus, lack of normalization

might have reduced the accuracy of the measurement when using a between-subject design. Normalization of MEPs is conducted by calculating a ratio between the raw EMG data collected from a muscle during a task and a reference value recorded from the same muscle. The reference EMG value can be the EMG value recorded during a maximal voluntary isometric muscle contraction (Burden, 2010). Alternatively, the reference value can be the maximal response recorded by electrically stimulating the muscle itself, called the M-max (see Section 7.2.5) (Keenan et al., 2006; Kidgell & Pearce, 2010). The current swallowing-related MEP literature does not indicate employment of normalization techniques. These approaches of normalization should be investigated when measuring MEPs from swallowing-related muscles.

PART V: FINAL REMARKS AND FUTURE RESEARCH

CHAPTER 10: FINAL REMARKS AND FUTURE RESEARCH

This research programme is the first to have assessed the application of swallowing skill training as a technique for improvement of swallowing precision. To thoroughly evaluate its effects in healthy subjects, investigation of neurophysiological, biomechanical, and muscular adaptations were included. In addition, biomechanical and muscular adaptations were evaluated in subjects with dysphagia secondary to PD. In summary, positive effects of treatment were found in the dysphagic group, but some indication of negative effects was identified in the healthy group. In addition, this is the first study to compare skill to strength training in swallowing. The only significant difference between the treatment groups was increased submental activity in effortful swallowing task following strength training but not skill training. Other differences found were dependent on interactions of age or gender with training type.

More specifically, skill training was proposed to result in neurophysiological adaptation leading to increased MEPs in functional swallowing but this hypothesis was not supported. However, younger subjects did demonstrate a marginally significant increase their submental activity in non-effortful swallowing task, which might be an indicator of neural adaptation occurring in the trained task that was not identified due to methodological limitations. Unexpectedly, reduced mid-pharyngeal pressure occurred in a subgroup of the skill training cohort. In addition, skill training resulted in decreased hyoid displacement and shorter UES opening in effortful tasks in males. Possibly, male subjects were increasing muscle power during training, including that of the pharyngeal musculature, due to the specification of the training protocol, which could be adjusted in future studies. Increased pharyngeal strength in healthy subjects might disrupt the fine balance that exists in activation of muscles attached to the hyoid, leading to its restricted movement.

Strength training led to an increase in sEMG peak amplitude in effortful swallowing tasks, manifested during and following the training. Females had decreased UES pressure and a trend towards longer UES opening. In addition, older subjects had a trend towards decreased UES opening duration. This trend should be further investigated in order to reach firm conclusions.

Skill training was also evaluated in a small group of individuals with dysphagia secondary to PD since this population was reported to benefit from external cues for motor function. There was support for positive changes, including increased submental activity in effortful swallowing tasks

following training. The same cohort of ten patients also had decreased swallowing pre-motor time, and shorter time in completing a continuous water swallowing task, with increased volume of each swallow, indicating improved swallowing efficiency (Athukorala, 2012).

In addition, high intensity training was included and a prolonged training period was evaluated, since there is evidence to support that changes are elicited following increased training dosage (Dobkin, 2005; Krakauer, Carmichael, Corbett, & Wittenberg, 2012). However, the small sample size did not allow for extraction of clear trends.

Overall, swallowing skill training appears to have considerable potential as a new approach in swallowing rehabilitation in individuals with dysphagia secondary to PD. Notwithstanding, further studies are needed to determine the efficacy and efficiency (Rosenbek, 1995) of both the skill and strength training paradigms.

10.1 Integration of results

Integration of the four studies included in this research programme reveals some issues that require further discussion.

10.1.1 The importance of Phase I research trials

The importance of conducting Phase I research trials is supported by this project. Although skill training with delayed feedback was found to improve motor function and enhance motor learning in non-swallowing research areas, its implementation in swallowing training in healthy subjects resulted in decreased pharyngeal pressure. This result has the potential to exacerbate swallowing impairment in individuals with dysphagia.

Another benefit of this Phase I trial is the observation that genders behave differently in response to training and further task development may need to accommodate this. Males had reduced hyoid displacement following skill training. The reduction in hyoid movement may have led to elevated nadir pressure in non-effortful saliva swallowing, and shorter UES opening in effortful tasks. In addition, young subjects in skill training had trends towards higher UES pressure and shorter opening. It is possible that male subjects and younger subjects in skill training increased their muscle power as a by-product of skill training within the 20-70% amplitude range for the target. This range might need to be reconsidered in future studies. However, it is important to bear in mind that just repeating the motor act of swallowing will not generate neural adaptation (Plautz et al., 2000). Thus, simply reducing the demand for a certain variation in strength might not be challenging enough for change to occur.

Following strength training, older subjects had a trend towards shorter UES opening. Since older individuals have a higher prevalence of stroke and are often prescribed with strength training for their dysphagia, this finding should be investigated further, as it has the underexplored potential for adverse effects in patients with dysphagia.

Effect sizes were calculated to provide estimation of potential effects of each training group, in order to calculate sample size in future studies, and to estimate whether a particular measure should be included in future studies in the clinical-trial series. Most effect sizes were found to be small in healthy subjects, with some exceptions (e.g., skill training had a medium effect size of increased pharyngeal pressure duration in non-effortful tasks and strength training had a large effect size indicating increase pharyngeal duration in effortful tasks). Measures with large effect size can support further investigation in healthy subjects. It is important to bear in mind that the indications of change found in healthy participants might not represent the expected result in subjects with dysphagia.

Lastly, it is important to emphasize that one should be aware that identification of negative effects in healthy individuals is important, however, as found in the treatment pilot study, the same training protocol can have different, and beneficial, effects in individuals with dysphagia. Hence, phase I trials in clinical research can, and should, include individuals with dysphagia attributed to a specific deficit, which can be alleviated by the offered treatment (Whyte et al., 2009).

10.1.2 *Interpretation of MEP magnitude*

The baseline study revealed age-related differences in submental MEP magnitude. Older subjects produced larger MEPs than younger subjects, indicating that age-related plastic adaptations occur and affect both volitional swallowing and volitional contraction. Regression analysis revealed that those changes occur gradually with age. Although the subjects in this study were healthy and presented no swallowing symptoms, age-related changes in skeletal muscles that are well documented (Berger & Doherty, 2010; Evans, 1995) can also affect the muscles involved in swallowing, and thus, changes in swallowing physiology may be detected in some healthy individuals (Robbins et al., 1992). Several questions arise. Is it possible that increased MEP magnitude following intervention constitutes a positive outcome in individuals with dysphagia but not in healthy subjects? Is there an ‘ultimate’ MEP size that allows normal function? Is the desirable outcome of swallowing training in older subjects an increase or a decrease in MEP magnitude? The answer to these questions depends on understanding the underlying cause for increased MEP in older subjects.

Rehabilitation-related studies consider increased MEP magnitude a positive outcome following therapy (Hamdy, Aziz, Rothwell, Crone, et al., 1997), and an absent or decreased MEP magnitude a negative predictor for motor improvement (Koski et al., 2004; Piron et al., 2005). Dysphagia recovery has been related to expansion of the pharyngeal cortical area in the intact hemisphere measured by increased MEP amplitude from additional areas in M1 (Hamdy, Aziz, Rothwell, Crone, et al., 1997). Limb movement recovery was found to have a positive correlation with MEP magnitude, however this correlation was dependent on the severity of the impairment, with larger MEPs immediately post injury serving as a positive predictor for recovery (Koski et al., 2004; Piron et al., 2005). Hence, increasing MEP magnitude and expanding M1 areas from which MEPs can be recorded is a positive outcome in persons with motor impairments following motor rehabilitation. However, it is unknown if larger measured MEPs are always better, particularly in a healthy population.

Interpretation of the integrated results from the baseline study (Chapter 9) that revealed greater swallowing-related submental MEPs in older subjects is not straightforward. The large magnitude of MEPs may reflect a compensatory mechanism for deterioration in function with age (Bernard & Seidler, 2012). Alternatively, large MEPs in older subjects might be ‘disabling’ as they might prevent precise and efficient movement execution (Zoghi et al., 2003). This is evident in reports from the literature regarding delayed pharyngeal swallowing (Logemann, 1990; Robbins et al., 1992) and increased prevalence of aspiration (Butler et al., 2011). These symptoms can be the result of imprecision leading to changes in swallowing function. Again, it is important to emphasize that changing physiology will not necessarily translate to dysphagia. Indeed, changes in MEP magnitude may not directly translate to changes in swallowing function (Power et al., 2004).

Furthermore, if the desirable outcome following intervention is to increase MEP magnitude (see hypotheses H4 and H5), it is not clear whether there is a certain level or threshold of MEPs that allow normal function. As stated in Chapter 6, older subjects continued to demonstrate greater MEPs in comparison to young subjects following training. If increased excitability is ‘destructive’ then training might exacerbated this as evidenced by strength training leading to a trend towards increased MEP magnitude in submental contraction. Based on the findings of the current study, older subjects engaged in strength training had a shorter UES opening in effortful saliva swallowing and increased submental activation in effortful swallowing tasks. The increase in MEP magnitude associated with submental contraction might be related to this finding. Thus, increased MEP magnitude might be a negative result for older subjects. If the neural adaptation demonstrated by older subjects has a ‘protective’ role (i.e., serving as a compensatory mechanism to maintain function), then skill training presumably maintained this, as no changes occurred in

functional saliva swallowing in skill training. The interpretation is again limited by the lack of basic knowledge regarding the nature of the ‘desirable’ outcome.

Increased MEPs magnitude in older subjects might be related to reduced inhibition. In this case, it is possible that training should aim to increase inhibition and, thus, reduce MEP magnitude. A study that measured cortical excitability during discrete activation of fingers found that intracortical inhibition is the mechanisms that allows selective activation of the fingers (Zoghi et al., 2003). Thus, increasing neural inhibition in older subjects might reflect neural adaptation that enables the motor command to be sent to the appropriate muscles only (Duchateau et al., 2006), and by that may hypothetically increase swallowing coordination. In a study of post-stroke patients, increased MEP magnitude was found prior to any training in the ipsilateral hemisphere. Following skill training of the upper limb, MEP magnitude from M1 of this hemisphere was reduced, which reflected a more normal activation pattern (Boyd et al., 2010). The reduction allowed for an efficient activation as manifested by increased performance ability (reduction in reaction time and movement time). Boyd et al.’s (2010) study might also support the possibility that reduction in MEP magnitude among the older subjects would be a positive outcome.

The fact that there is a lack of knowledge towards the expected outcome is of concern, since MEPs are frequently used as a tool to assess neurophysiological integrity and changes in excitability following training. This project highlights this lack of understanding. There is a need to conduct methodological studies in order to understand what constitutes a normal and positive outcome and what constitutes an impaired and negative outcome.

Gender effects on MEP magnitude

The gender effect found in swallowing-MEPs post 10th training session, whereby females had larger MEPs than males, was not found at baseline. The disproportionate increase in submental MEP magnitude in females during swallowing might be related to the non-significant increase in hyoid displacement during swallowing in this group following training. This difference might suggest that increased hyoid displacement was related to increase efferent downflow, manifested as increase MEP magnitude and as improved synchronization of motor units firing, and higher firing frequency of the submental motor units that led to increased pull of the hyoid bone forward. On the other hand, the lack of gender effects in submental muscle activity as measured by sEMG, does not support this suggestion. Overall, there were no differences between genders in MEP changes measured 4 days following training, hence both genders demonstrated similar neural adaptations to training.

10.1.3 *The principle of initial values*

The principle of initial values states that individuals with lower initial values in motor performance have a greater capacity for change following intervention. This was found in the main study (Chapter 6) and in the pilot study that consisted of individuals with PD (Chapter 8).

In the main study, older females and young males had a greater degree of change following training in comparison with young females and older males. The study by Youmans et al. (2009) discussed in Chapter 7 provides support for this hypothesis. Similarly, comparing the results of the PD group with those of the healthy subjects, while taking into account baseline differences, led to a different, and perhaps more accurate, interpretation of the training effects in the PD group. The dysphagic group had lower baseline values of submental sEMG peak amplitude in the effortful swallowing task, but not during non-effortful tasks, in comparison to the non-dysphagic group, while considering age as a covariate. Following skill training with immediate feedback, the dysphagic group had an increase in submental activity in the effortful swallowing task but not in non-effortful swallowing task, in comparison to the non-dysphagic group (Chapter 8). This finding emphasizes that changes will occur if there is a capacity for potential improvement.

10.1.4 *Dysphagia secondary to Parkinson's disease*

As discussed by Aydogdu et al. (2011), although swallowing disorders have been described in PD, we still do not understand the nature of dysphagia secondary to this disorder. There is a need to better understand the specific swallowing mechanisms that are impaired, in comparison to age-matched controls. For example, although there is a debate regarding limb weakness in PD as being a primary or secondary symptom (Morris et al., 2010), the presence of weakness is investigated and assessed and, hence, leads to better understanding of the deficits associated with PD. Physical therapy which emphasizes strength training is available for patients and provides beneficial results (Falvo et al., 2008). In swallowing-related research, weakness is not assessed nor described in individuals with dysphagia secondary to PD. Without understanding the specific characteristics of dysphagia secondary to PD, it is difficult to design specific programmes to answer the needs of this population. The results presented in Chapter 8 demonstrate that individuals with dysphagia secondary to PD have decreased submental activity in effortful tasks in comparison to non-dysphagic subjects. Reduced submental muscle group activity detected in effortful tasks might influence other functional deficits that can be related to this muscle group, like hyoid excursion. Interestingly, only one study demonstrated a difference in hyoid displacement in PD versus controls. The difference was attributed to hypokinesia, with elevated hyoid position at the start of the swallow in comparison to healthy controls (Wintzen, Badrising,

Roos, Vielvoye, & Liauw, 1994). Other than the Wintzen et al.'s (1994) study, other studies (Bird et al., 1994; Fuh et al., 1997; Leopold & Kagel, 1997) described hyoid dysfunction-related symptoms in PD like pyriform sinus residuals. However, since pyriform sinus residuals can also result from other causes like malfunctioning UES, the symptom description alone cannot help in describing function and dysfunction. There is a need for a thorough evaluation of dysphagia in PD. This can lead to adjustments to the training protocol of swallowing skill training that was implemented in the PD group to further improve swallowing function.

10.2 Future research

Main study

This study constituted a Phase I clinical-trial that aimed to assess safety, methods, outcome measures, and effect sizes. Additional Phase I research trials are still needed to clarify safety as revealed by this study. Future research in Phase I clinical-trial could consist of another population of patients with dysphagia, such as individuals with dysphagia secondary to cortical or brainstem stroke.

Since swallowing is bilaterally innervated by the cortex, future studies should include M1 mapping of both hemispheres as an outcome measure. In addition, since one hemisphere usually contains the hotspot (i.e., corticobulbar projects to the muscles characterized by high MEP amplitude), and the other has an area that sends projections that are of lower magnitude, evaluation of the latter can teach us about changes to that area. This would be of interest, since it is possible that training affect neural control in both hemispheres. Another modification to the MEP assessment protocol worth consideration would be to localize contraction-related and swallowing-related hotspots in a separate baseline study. If two areas are found consistently, then training effects strictly need to be measured in both areas. In addition, including pharyngeal and oesophageal MEP assessment as an outcome measure could reveal changes in cortical control following swallowing training.

The effects of training on hyoid displacement in males following skill training should be further investigated using a larger sample size that will allow an accurate assessment of gender effects on the outcomes of different training protocols. The effects of skill training on the UES in younger subjects should also be further investigated. It is possible that only one of the skill protocols resulted in decreased hyoid displacement. Hence, skill training protocols should be investigated with sufficient sample size that will allow evaluation of gender and age effects. In addition, increased statistical power is required to evaluate the effects of skill training with immediate feedback and skill training with delayed feedback on neurophysiological adaptations. It is quite

possible that modification of the MEP assessment methods, such as locating the swallowing-related hotspot and bilateral M1 mapping, would reveal neural adaptations for swallowing execution.

The trends towards shorter UES opening in older subjects following strength training should also be evaluated further. This is important as strength training is frequently prescribed to patients in clinical settings, and these possible negative effects should be better understood.

Different training protocols could be employed in future studies. For example, since following skill training males had reduced hyoid movement, and younger subjects had a trend towards increased UES pressure, future studies can test if reduced demand for force during training (e.g., 20-60% instead of 20-70% of maximal contraction) would have similar effects on hyoid movement. In addition, an extended training period can be employed, with measurements taken throughout the training period. For example, a 6-week training period can be employed with measurements taken every 2 weeks post-training onset, with additional assessments taking place 2 weeks post training to evaluate maintenance. It is also possible that as skill training continues, the initial target size should be decreased (i.e., instead of 50% of the amplitude area calculated at the beginning of the session as described in Section 5.3.2, 40% or 30% should be used to calculate the initial target size). This might represent a task that increases the demand for precision at the very start of the session, rather than gradually increasing it.

In order to assess changes in muscle activity following training, a future study can utilize intramuscular EMG electrodes, with cross correlation technique to assess synchronization by measuring discharge time from a pair of motor units that are concurrently active. Alternatively, a linear electrode array of sEMG electrodes connected to multiple recording channels has the potential to give reliable information for detecting motor unit and muscle fibre properties like conduction velocity and muscle fatigue.

Swallowing disorders secondary to PD

Since positive outcomes were indicated following skill training in subjects with dysphagia secondary to PD, a future study should employ a larger cohort of patients with PD, and compare the results between a sham group and a training group. In addition, a larger sample is needed to increase statistical power and evaluate changes in motor performance (target hit-rate) during training.

Changes in swallowing function were found in this cohort of subjects (Athukorala, 2012) indicating more efficient swallowing execution. Employing manofluoroscopy for swallowing function assessment would allow thorough investigation of functional improvement following

swallowing skill training. In addition, only biomechanical assessments were conducted, thus, it would have been beneficial to investigate changes in MEP following training in this population. A future study should consider undertaking a broad assessment approach that will include investigation of neural adaptations.

Although no differences were found between healthy subjects and individuals with dysphagia secondary to PD in submental activity associated with non-effortful swallowing tasks, a future study should challenge non-effortful functional swallowing by introducing continuous swallowing tasks. The task can involve boli of complex texture and of various sizes for continuous swallowing, while measuring submental activity. The outcomes can be compared between persons with dysphagia secondary to PD and healthy controls. Since decreased muscle reserve was found in the dysphagic group in comparison to the non-dysphagic group, the PD group might demonstrate differences in functions that are important to detect.

Age-related differences in MEP

Data from the current study emphasized the importance of using different reference points for evaluation of MEPs for each age group. These age-related differences in MEP size should be taken into consideration when designing future research.

The role of swallowing-related neural inhibition in healthy subjects is of interest. In addition, evaluating training-related changes in interhemispheric inhibition could provide useful information. A future study could employ an inhibitory paired-pulse protocol and measure intracortical inhibition of M1 projections to the submental muscles, as a function of age. Since the submental area is bilaterally innervated (Hamdy et al., 1996; Sowman et al., 2009) paired-pulse TMS can be conducted by delivering both pulses to one hemisphere, to both hemispheres at the same time, or by delivering the conditioning pulse to one hemisphere and the unconditioned pulse to the other (Wassermann et al., 2008).

Age-related peripheral changes could be reflected as increased MEP due to ‘exaggerated’ recruitment of larger motor units. Age-related central changes could reflect over activation due to decreased inhibition, which would result in ‘exaggerated’ recruitment of brain areas leading to increased neural downflow. A possible way to tease apart central from peripheral mechanisms would be to normalize the MEP to a measure of peripheral propagation. However, no swallowing-related study has yet utilized such a method. A future study should explore the possibility of implementing normalization techniques for the swallowing musculature.

In addition, assessing the swallowing muscles force and activation during swallowing by integrating biomechanical measures, concurrent with neurophysiological measures, like MEP

magnitude from related swallowing muscles, could give important insight into the possibility of positive relationship between larger MEP and increased effort.

Lastly, a baseline study should be conducted, consisting of a large sample size of individuals aged 50 years and above, with no swallowing difficulties and individuals with swallowing difficulties that are unrelated to neurological or structural disorders. Evaluation of the neural output should be conducted concurrently with biomechanical assessments like pharyngeal manometry EMG activation from swallowing-related muscles. Functional swallowing should also be assessed. This would reveal a possible correlation between the measurements, and a better understanding of the role of increased MEPs in older subjects.

REFERENCES

- Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, P., & Dyhre-Poulsen, P. (2002). Increased rate of force development and neural drive of human skeletal muscle following resistance training. *Journal of Applied Physiology*, 93(4), 1318–1326.
- Abdul Wahab, N., Jones, R. D., & Huckabee, M. L. (2010). Effects of olfactory and gustatory stimuli on neural excitability for swallowing. *Physiology & Behavior*, 101(5), 568–575. Elsevier Inc.
- Adkins, D. L., Boychuk, J., Remple, M. S., & Kleim, J. A. (2006). Motor training induces experience-specific patterns of plasticity across motor cortex and spinal cord. *Journal of Applied Physiology*, 101(6), 1776–1782.
- Al-Toubi, A. K., Abu-Hijleh, A., Huckabee, M. L., Macrae, P., & Doeltgen, S. H. (2011). Effects of repeated volitional swallowing on the excitability of submental corticobulbar motor pathways. *Dysphagia*, 26(3), 311–317.
- Alberts, M. J., Horner, J., Gray, L., & Brazer, S. R. (1992). Aspiration after stroke: lesion analysis by brain MRI. *Dysphagia*, 7(3), 170–173.
- Aldridge, K. J., & Taylor, N. F. (2012). Dysphagia is a common and serious problem for adults with mental illness: a systematic review. *Dysphagia*, 27(1), 124–137.
- Alhashemi, H. H. (2010). Dysphagia in severe traumatic brain injury. *Neurosciences (Riyadh, Saudi Arabia)*, 15(4), 231–236.
- Ali, G. N., Wallace, K. L., Schwartz, R., DeCarle, D. J., Zagami, A. S., & Cook, I. J. (1996). Mechanisms of oral-pharyngeal dysphagia in patients with Parkinson's disease. *Gastroenterology*, 110(2), 383–392.
- Allen, J., White, C. J., Leonard, R. J., & Belafsky, P. C. (2010). Prevalence of penetration and aspiration on videofluoroscopy in normal individuals without dysphagia. *Otolaryngology - Head and Neck Surgery*, 142(2), 208–213.
- Allen, N. E., Canning, C. G., Sherrington, C., & Fung, V. S. C. (2009). Bradykinesia, muscle weakness and reduced muscle power in Parkinson's disease. *Movement Disorders*, 24(9), 1344–1351.
- Allen, N. E., Sherrington, C., Canning, C. G., & Fung, V. S. C. (2010). Reduced muscle power is associated with slower walking velocity and falls in people with Parkinson's disease. *Parkinsonism & Related Disorders*, 16(4), 261–264. Elsevier Ltd.
- Amassian, V. E., Stewart, M., Quirk, G. J., & Rosenthal, J. L. (1987). Physiological basis of motor effects of a transient stimulus to cerebral cortex. *Neurosurgery*, 20(1), 74–93.
- American Speech-Language-Hearing Association. (2010). Code of Ethics. www.asha.org/policy.
- Aminpour, S., Leonard, R. J., Fuller, S. C., & Belafsky, P. C. (2011). Pharyngeal wall differences between normal younger and older adults. *Ear, Nose, & Throat Journal*, 90(4), E1.
- Anand, S., & Hotson, J. (2002). Transcranial magnetic stimulation: neurophysiological applications and safety. *Brain and Cognition*, 50(3), 366–386.

- Arabadzhev, T. I., Dimitrov, G. V., Chakarov, V. E., Dimitrov, A. G., & Dimitrova, N. A. (2008). Effects of changes in intracellular action potential on potentials recorded by single-fiber, macro, and belly-tendon electrodes. *Muscle & Nerve*, 37(6), 700–712.
- Arabadzhev, T. I., Dimitrov, V. G., Dimitrova, N. A., & Dimitrov, G. V. (2010). Influence of motor unit synchronization on amplitude characteristics of surface and intramuscularly recorded EMG signals. *European Journal of Applied Physiology*, 108(2), 227–237.
- Arima, T., Yanagi, Y., Niddam, D. M., Ohata, N., Arendt-Nielsen, L., Minagi, S., Sessle, B. J., et al. (2011). Corticomotor plasticity induced by tongue-task training in humans: a longitudinal fMRI study. *Experimental Brain Research*, 212(2), 199–212.
- Athukorala, R. (2012). *Skill training for swallowing rehabilitation in individuals with Parkinson's disease*. Master's thesis, University of Canterbury, Christchurch, New Zealand.
- Aviv, J. E., Martin, J. H., Jones, M. E., Wee, T. A., Diamond, B., Keen, M. S., & Blitzer, A. (1994). Age-related changes in pharyngeal and supraglottic sensation. *The Annals of Otolaryngology, Rhinology & Laryngology*, 103(10), 749–752.
- Aydogdu, I., Tanriverdi, Z., & Ertekin, C. (2011). Dysfunction of bulbar central pattern generator in ALS patients with dysphagia during sequential deglutition. *Clinical Neurophysiology*, 122(6), 1219–1228. International Federation of Clinical Neurophysiology.
- Aziz, Q., Rothwell, J. C., Barlow, J., Hobson, A., Alani, S., Bancewicz, J., & Thompson, D. G. (1994). Esophageal myoelectric responses to magnetic stimulation of the human cortex and the extracranial vagus nerve. *The American Journal of Physiology*, 267(5 Pt 1), G827–835.
- Baijens, L. W. J., & Speyer, R. (2009). Effects of therapy for dysphagia in Parkinson's disease: systematic review. *Dysphagia*, 24(1), 91–102.
- Baine, W. B., Yu, W., & Summe, J. P. (2001). Epidemiologic trends in the hospitalization of elderly Medicare patients for pneumonia, 1991-1998. *American Journal of Public Health*, 91(7), 1121–1123.
- Baker, S., Davenport, P., & Sapienza, C. (2005). Examination of strength training and detraining effects in expiratory muscles. *Journal of Speech, Language, and Hearing Research*, 48(6), 1325–33.
- Banneheka, S. (2008). Anatomy of the ansa cervicalis: Nerve fiber analysis. *Anatomical Science International*, 83(2), 61–67. Wiley Online Library.
- Barker, A. T. (1999). The history and basic principles of magnetic nerve stimulation. *Electroencephalography and Clinical Neurophysiology*, 51, 3–21.
- Barker, A. T., Jalinous, R., & Freeston, I. L. (1985). Non-invasive magnetic stimulation of human motor cortex. *Lancet*, 1(8437), 1106–7.
- Barlow, S. M. (1999). *Handbook of clinical speech physiology*. San Diego, CA: Singular Thomson Learning.
- Barlow, S. M., & Netsell, R. (1986). Differential fine force control of the upper and lower lips. *Journal of Speech and Hearing Research*, 29(2), 163–169.

- Barnett, M. L., Ross, D., Schmidt, R. A., & Todd, B. (1973). Motor skills learning and the specificity of training principle. *Research Quarterly*, 44(4), 440–447.
- Barofsky, I. (1995). Surface electromyographic biofeedback and the patient with dysphagia: clinical opportunities and research questions. *Dysphagia*, 10(1), 19–21.
- Basmajian, J. V. (1989). *Biofeedback: principles and practice for clinician* (3rd Ed.). Baltimore: Williams & Wilkins.
- Bath, P. M., Bath, F. J., & Smithard, D. G. (2000). Interventions for dysphagia in acute stroke. *Cochrane Database of Systematic Reviews (Online)*, (2), CD000323.
- Beckstead, R. M., Morse, J. R., & Norgren, R. (1980). The nucleus of the solitary tract in the monkey: projections to the thalamus and brain stem nuclei. *The Journal of Comparative Neurology*, 190(2), 259–282.
- Belafsky, P. C., Mouadeb, D. A., Rees, C. J., Pryor, J. C., Postma, G. N., Allen, J., & Leonard, R. J. (2008). Validity and reliability of the Eating Assessment Tool (EAT-10). *The Annals of Otolaryngology, Rhinology, and Laryngology*, 117(12), 919–924.
- Bergdahl, M. (2000). Salivary flow and oral complaints in adult dental patients. *Community Dentistry and Oral Epidemiology*, 28(1), 59–66.
- Berger, M. J., & Doherty, T. J. (2010). Sarcopenia: prevalence, mechanisms, and functional consequences. *Interdisciplinary Topics in Gerontology*, 37, 94–114.
- Bernard, J. a, & Seidler, R. D. (2012). Evidence for motor cortex dedifferentiation in older adults. *Neurobiology of Aging*, 33(9), 1890–9. Elsevier Inc.
- Bhogal, S. K., Teasell, R. W., & Speechley, M. (2003). Intensity of aphasia therapy, impact on recovery. *Stroke*, 34(4), 987–993.
- Bienenstock, E. L., Cooper, L. N., & Munro, P. W. (1982). Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex. *The Journal of Neuroscience*, 2(1), 32–48.
- Biernaskie, J., Chernenko, G., & Corbett, D. (2004). Efficacy of rehabilitative experience declines with time after focal ischemic brain injury. *The Journal of Neuroscience*, 24(5), 1245–1254.
- Bine, J. E., Frank, E. M., & McDade, H. L. (1995). Dysphagia and dementia in subjects with Parkinson's disease. *Dysphagia*, 10(3), 160–164.
- Binkofski, F., Schnitzler, A., Enck, P., Frieling, T., Posse, S., Seitz, R. J., & Freund, H. J. (1998). Somatic and limbic cortex activation in esophageal distention: a functional magnetic resonance imaging study. *Annals of Neurology*, 44(5), 811–815.
- Bird, M. R., Woodward, M. C., Gibson, E. M., Phyland, D. J., & Fonda, D. (1994). Asymptomatic swallowing disorders in elderly patients with Parkinson's disease: a description of findings on clinical examination and videofluoroscopy in sixteen patients. *Age and Ageing*, 23(3), 251–254.
- Black, J. E., Isaacs, K. R., Anderson, B. J., Alcantara, A. A., & Greenough, W. T. (1990). Learning causes synaptogenesis, whereas motor activity causes angiogenesis, in cerebellar

- cortex of adult rats. *Proceedings of the National Academy of Sciences of the United States of America*, 87(14), 5568–5572.
- Blazevich, A. J., Gill, N. D., Deans, N., & Zhou, S. (2007). Lack of human muscle architectural adaptation after short-term strength training. *Muscle & Nerve*, 35(1), 78–86.
- Bloem, B. R., Lagaay, A. M., van Beek, W., Haan, J., Roos, R. A., & Wintzen, A. R. (1990). Prevalence of subjective dysphagia in community residents aged over 87. *British Medical Journal*, 300(6726), 721–722.
- Bloxham, C. A., Mindel, T. A., & Frith, C. D. (1984). Initiation and execution of predictable and unpredictable movements in Parkinson's disease. *Brain*, 107, 371–384.
- Borges, A., & Casselman, J. (2010). Imaging the trigeminal nerve. *European Journal of Radiology*, 74(2), 323–340. Elsevier Ireland Ltd.
- Borggreven, P. A., Verdonck-de Leeuw, I., Rinkel, R. N., Langendijk, J. A., Roos, J. C., David, E. F. L., de Bree, R., et al. (2007). Swallowing after major surgery of the oral cavity or oropharynx: a prospective and longitudinal assessment of patients treated by microvascular soft tissue reconstruction. *Head & Neck*, 29(7), 638–347.
- Boroojerdi, B., Foltys, H., Krings, T., Spetzger, U., Thron, A., & Töpper, R. (1999). Localization of the motor hand area using transcranial magnetic stimulation and functional magnetic resonance imaging. *Clinical Neurophysiology*, 110(4), 699–704.
- Bothe, A. K., & Richardson, J. D. (2011). Statistical, practical, clinical, and personal significance: definitions and applications in speech-language pathology. *American Journal of Speech-Language Pathology*, 20(3), 233–242.
- Boudreau, S., Romaniello, A., Wang, K., Svensson, P., Sessle, B. J., & Arendt-Nielsen, L. (2007). The effects of intra-oral pain on motor cortex neuroplasticity associated with short-term novel tongue-protrusion training in humans. *Pain*, 132(1-2), 169–178.
- Bourbonnais, D., Bilodeau, S., Lepage, Y., Beaudoin, N., Gravel, D., & Forget, R. (2002). Effect of force-feedback treatments in patients with chronic motor deficits after a stroke. *American Journal of Physical Medicine & Rehabilitation*, 81(12), 890–897.
- Boyd, L. A., Vidoni, E. D., & Wessel, B. D. (2010). Motor learning after stroke: is skill acquisition a prerequisite for contralesional neuroplastic change? *Neuroscience*, 482(1), 21–5. Elsevier Ireland Ltd.
- Brackmann, D. E., & Fetterman, B. . (2007). Cranial nerve VII: Facial nerve. In C. G. Goetz (Ed.), *Textbook of Clinical Neurology* (3rd Ed., pp. 185–198). Philadelphia, PA: Elsevier Inc.
- Brasseur, J. G., & Dodds, W. J. (1991). Interpretation of intraluminal manometric measurements in terms of swallowing mechanics. *Dysphagia*, 6(2), 100–119.
- Breteler, M. M., Claus, J. J., van Duijn, C. M., Launer, L. J., & Hofman, A. (1992). Epidemiology of Alzheimer's disease. *Epidemiologic reviews*, 14, 59–82.

- Brockmann, K., Becker, P., Schreiber, G., Neubert, K., Brunner, E., & Bönnemann, C. (2007). Sensitivity and specificity of qualitative muscle ultrasound in assessment of suspected neuromuscular disease in childhood. *Neuromuscular Disorders*, 17(7), 517–723.
- Broussard, D. L., & Altschuler, S. M. (2000). Central integration of swallow and airway-protective reflexes. *The American Journal of Medicine*, 108(4a), 62S–67S.
- Bruechert, L., Lai, Q., & Shea, C. H. (2003). Reduced knowledge of results frequency enhances error detection. *Research Quarterly for Exercise and Sport*, 74(4), 467–472.
- Bryant, M. (1991). Biofeedback in the treatment of a selected dysphagic patient. *Dysphagia*, 6(3), 140–144.
- Buetow, S., Giddings, L. S., Williams, L., & Nayar, S. (2008). Perceived unmet needs for health care among Parkinson's Society of New Zealand members with Parkinson's disease. *Parkinsonism & Related Disorders*, 14(6), 495–500.
- Burden, A. (2010). How should we normalize electromyograms obtained from healthy participants? What we have learned from over 25 years of research. *Journal of Electromyography and Kinesiology*, 20(6), 1023–35.
- Burkhead, L. M., Sapienza, C. M., & Rosenbek, J. C. (2007). Strength-training exercise in dysphagia rehabilitation: principles, procedures, and directions for future research. *Dysphagia*, 22(3), 251–265.
- Bushmann, M., Dobmeyer, S. M., Lecker, L., & Perlmuter, J. S. (1989). Swallowing abnormalities and their response to treatment in Parkinson's disease. *Neurology*, 39(10), 1309–1314.
- Butler, S. G., Stuart, A., Castell, D. O., Russell, G. B., Koch, K., & Kemp, S. (2009). Effects of age, gender, bolus condition, viscosity, and volume on pharyngeal and upper esophageal sphincter pressure and temporal measurements during swallowing. *Journal of Speech, Language, and Hearing Research*, 52(1), 240–253. ASHA.
- Butler, S. G., Stuart, A., Leng, X., Wilhelm, E., Rees, C., Williamson, J., & Kritchevsky, S. B. (2011). The relationship of aspiration status with tongue and handgrip strength in healthy older adults. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 66(4), 452–8.
- Butler, S. L., Miles, T. S., Thompson, P. D., & Nordstrom, M. A. (2001). Task-dependent control of human masseter muscles from ipsilateral and contralateral motor cortex. *Experimental Brain Research*, 137(1), 65–70.
- Byrnes, M. L., Thickbroom, G. W., Phillips, B. A., & Mastaglia, F. L. (2001). Long-term changes in motor cortical organisation after recovery from subcortical stroke. *Brain Research*, 889(1-2), 278–287.
- Bülow, M., Olsson, R., & Ekberg, O. (1999). Videomanometric analysis of supraglottic swallow, effortful swallow, and chin tuck in healthy volunteers. *Dysphagia*, 14(2), 67–72.
- Bülow, M., Olsson, R., & Ekberg, O. (2001). Videomanometric analysis of supraglottic swallow, effortful swallow, and chin tuck in patients with pharyngeal dysfunction. *Dysphagia*, 16(3), 190–195.

- Bülow, M., Olsson, R., & Ekberg, O. (2002). Supraglottic swallow, effortful swallow, and chin tuck did not alter hypopharyngeal intrabolus pressure in patients with pharyngeal dysfunction. *Dysphagia*, 17(3), 197–201.
- Bütefisch, C., Hummelsheim, H., Denzler, P., & Mauritz, K. H. (1995). Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally parietic hand. *Journal of the neurological sciences*, 130(1), 59–68.
- Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: the HAROLD model. *Psychology and Aging*, 17(1), 85–100.
- Calcagno, P., Ruoppolo, G., Grasso, M. G., De Vincentiis, M., & Paolucci, S. (2002). Dysphagia in multiple sclerosis - prevalence and prognostic factors. *Acta Neurologica Scandinavica*, 105(1), 40–43.
- Calder, K. M., Stashuk, D. W., & McLean, L. (2008). Physiological characteristics of motor units in the brachioradialis muscle across fatiguing low-level isometric contractions. *Journal of Electromyography and Kinesiology*, 18(1), 2–15.
- Cano-de-la-Cuerda, R., Pérez-de-Heredia, M., Miangolarra-Page, J. C., Muñoz-Hellín, E., & Fernández-de-Las-Peñas, C. (2010). Is there muscular weakness in Parkinson's disease? *American Journal of Physical Medicine & Rehabilitation*, 89(1), 70–76.
- Carnaby-Mann, G. D., & Crary, M. A. (2008). Adjunctive neuromuscular electrical stimulation for treatment-refractory dysphagia. *The Annals of Otolaryngology, Rhinology, and Laryngology*, 117(4), 279–287.
- Carnaby-Mann, G. D., & Crary, M. A. (2010). McNeill dysphagia therapy program: a case-control study. *Archives of Physical Medicine and Rehabilitation*, 91(5), 743–749. Elsevier Inc.
- Carroll, T. J., Riek, S., & Carson, R. G. (2002). The sites of neural adaptation induced by resistance training in humans. *The Journal of Physiology*, 544(2), 641–652. Adis International.
- Castell, J. A., & Castell, D. O. (1993). Modern solid state computerized manometry of the pharyngo-esophageal segment. *Dysphagia*, 8(3), 270–275.
- Chandler, J. M., Duncan, P. W., Kochersberger, G., & Studenski, S. (1998). Is lower extremity strength gain associated with improvement in physical performance and disability in frail, community-dwelling elders? *Archives of Physical Medicine and Rehabilitation*, 79(1), 24–30.
- Charlesworth, J. D., Warren, T. L., & Brainard, M. S. (2012). Covert skill learning in a cortical-basal ganglia circuit. *Nature*, 486(7402), 251–255. Nature Publishing Group.
- Chen, C.-M., & Huang, T.-Y. (2008). Lateral medullary infarction presenting contralateral palatal paresis. *Acta Neurologica Taiwanica*, 17(4), 239–242.
- Chhabra, A., & Sapienza, C. (2007). A review of neurogenic and myogenic adaptations associated with specific exercise. *Communicative Disorders Review*, 1(3-4), 175–194.

- Chi-Fishman, G. (2005). Quantitative lingual, pharyngeal and laryngeal ultrasonography in swallowing research: A technical review. *Clinical Linguistics & Phonetics*, 19(6-7), 589–604.
- Chi-Fishman, G., Hicks, J. E., Cintas, H. M., Sonies, B. C., & Gerber, L. H. (2004). Ultrasound imaging distinguishes between normal and weak muscle. *Archives of Physical Medicine and Rehabilitation*, 85(6), 980–986.
- Chi-Fishman, G., & Sonies, B. C. (2002a). Kinematic strategies for hyoid movement in rapid sequential swallowing. *Journal of Speech, Language, and Hearing Research*, 45(3), 457–468. ASHA.
- Chi-Fishman, G., & Sonies, B. C. (2002b). Effects of systematic bolus viscosity and volume changes on hyoid movement kinematics. *Dysphagia*, 17(4), 278–287.
- Chiara, T., Martin, D., & Sapienza, C. (2007). Expiratory muscle strength training: speech production outcomes in patients with multiple sclerosis. *Neurorehabilitation and Neural Repair*, 21(3), 239–249.
- Chitkara, A. E. (2006). Neuroanatomy of the larynx. In L. Sulica & A. Blitze (Eds.), *Vocal fold paralysis* (pp. 3–16). Berlin: Springer.
- Chokroverty, S., Hening, W., Wright, D., Walczak, T., Goldberg, J., Burger, R., Belsh, J., et al. (1995). Magnetic brain stimulation: safety studies. *Electroencephalography and Clinical Neurophysiology*, 97(1), 36–42.
- Chouinard, J., Lavigne, E., & Villeneuve, C. (1998). Weight loss, dysphagia, and outcome in advanced dementia. *Dysphagia*, 13(3), 151–155.
- Chua, K. S., & Kong, K. H. (1996). Functional outcome in brain stem stroke patients after rehabilitation. *Archives of Physical Medicine and Rehabilitation*, 77(2), 194–197.
- Cicinelli, P., Traversa, R., & Rossini, P. M. (1997). Post-stroke reorganization of brain motor output to the hand: a 2-4 month follow-up with focal magnetic transcranial stimulation. *Electroencephalography and Clinical Neurophysiology*, 105(6), 438–450.
- Cirillo, J., Todd, G., & Semmler, J. G. (2011). Corticomotor excitability and plasticity following complex visuomotor training in young and old adults. *The European Journal of Neuroscience*, 34(11), 1847–1856.
- Clark, H. M. (2003). Neuromuscular treatments for speech and swallowing: a tutorial. *American Journal of Speech-Language Pathology*, 12(4), 400–415.
- Clark, H. M., Henson, P. a, Barber, W. D., Stierwalt, J. a G., & Sherrill, M. (2003). Relationships among subjective and objective measures of tongue strength and oral phase swallowing impairments. *American Journal of Speech-Language Pathology*, 12(1), 40–50.
- Classen, J., Knorr, U., Werhahn, K. J., Schlaug, G., Kunesch, E., Cohen, L. G., Seitz, R. J., et al. (1998). Multimodal output mapping of human central motor representation on different spatial scales. *The Journal of Physiology*, 512(1), 163–179.

- Classen, J., Witte, O. W., Schlaug, G., Seitz, R. J., Holthausen, H., & Benecke, R. (1995). Epileptic seizures triggered directly by focal transcranial magnetic stimulation. *Electroencephalography and Clinical Neurophysiology*, 94(1), 19–25.
- Coates, C., & Bakheit, A. M. (1997). Dysphagia in Parkinson's disease. *European Neurology*, 38(1), 49–52.
- Cohen, H. (1999). *Neuroscience for Rehabilitation* (2nd Ed.). Philadelphia, PA: Lippincott Williams & Wilkins.
- Cohen, L. G., Roth, B. J., Nilsson, J., Dang, N., Panizza, M., Bandinelli, S., Friauf, W., et al. (1990). Effects of coil design on delivery of focal magnetic stimulation. Technical considerations. *Electroencephalography and Clinical Neurophysiology*, 75(4), 350–357.
- Colcombe, S. J., Kramer, A. F., Erickson, K. I., & Scalf, P. (2005). The implications of cortical recruitment and brain morphology for individual differences in inhibitory function in aging humans. *Psychology and Aging*, 20(3), 363–375.
- Colton-Hudson, A., Koopman, W. J., Moosa, T., Smith, D., Bach, D., & Nicolle, M. (2002). A prospective assessment of the characteristics of dysphagia in myasthenia gravis. *Dysphagia*, 17(2), 147–151.
- Comery, T. A., Shah, R., & Greenough, W. T. (1995). Differential rearing alters spine density on medium-sized spiny neurons in the rat corpus striatum: evidence for association of morphological plasticity with early response gene expression. *Neurobiology of Learning and Memory*, 63(3), 217–219.
- Cook, I. J. (2008). Diagnostic evaluation of dysphagia. *Nature Clinical Practice. Gastroenterology & Hepatology*, 5(7), 393–403.
- Cook, I. J., Dodds, W. J., Dantas, R. O., Kern, M. K., Massey, B. T., Shaker, R., & Hogan, W. J. (1989). Timing of videofluoroscopic, manometric events, and bolus transit during the oral and pharyngeal phases of swallowing. *Dysphagia*, 4(1), 8–15.
- Coutinho, S. B., Diaféria, G., Oliveira, G., & Behlau, M. (2009). Voice and speech of individuals with Parkinson s Disease during amplification, delay and masking situations. *Pró-Fono*, 21(3), 219–224.
- Cowan, J. M., Day, B. L., Marsden, C., & Rothwell, J. C. (1986). The effect of percutaneous motor cortex stimulation on H reflexes in muscles of the arm and leg in intact man. *The Journal of Physiology*, 377, 333–347.
- Crary, M. A. (1995). A direct intervention program for chronic neurogenic dysphagia secondary to brainstem stroke. *Dysphagia*, 10(1), 6–18.
- Crary, M. A., & Baldwin, B. O. (1997). Surface electromyographic characteristics of swallowing in dysphagia secondary to brainstem stroke. *Dysphagia*, 12(4), 180–187. Springer.
- Crary, M. A., Carnaby-Mann, G. D., & Groher, M. E. (2006). Biomechanical correlates of surface electromyography signals obtained during swallowing by healthy adults. *Journal of Speech, Language, and Hearing Research*, 49(1), 186–193.

- Crary, M. A., Carnaby-Mann, G. D., & Groher, M. E. (2007). Identification of swallowing events from sEMG Signals Obtained from Healthy Adults. *Dysphagia*, 22(2), 94–99.
- Crary, M. A., Carnaby-Mann, G. D., Groher, M. E., & Helseth, E. (2004). Functional benefits of dysphagia therapy using adjunctive sEMG biofeedback. *Dysphagia*, 19(3), 160–164.
- Cunning, D. M., Lipke, N., & Wax, M. K. (1998). Significance of unilateral submandibular gland excision on salivary flow in noncancer patients. *The Laryngoscope*, 108(6), 812–815.
- Cunnington, R., Iansek, R., Bradshaw, J. L., & Phillips, J. G. (1995). Movement-related potentials in Parkinson's disease. Presence and predictability of temporal and spatial cues. *Brain*, 118(4), 935–950.
- Cunnington, R., Iansek, R., Bradshaw, J. L., & Phillips, J. G. (1996). Movement-related potentials associated with movement preparation and motor imagery. *Experimental Brain Research*, 111(3), 429–436.
- Cunnington, R., Iansek, R., Johnson, K. A., & Bradshaw, J. L. (1997). Movement-related potentials in Parkinson's disease. Motor imagery and movement preparation. *Brain*, 120(8), 1339–1353.
- Van Cutsem, M., Duchateau, J., & Hainaut, K. (1998). Changes in single motor unit behaviour contribute to the increase in contraction speed after dynamic training in humans. *The Journal of physiology*, 513(1), 295–305.
- Dalgas, U. (2011). Rehabilitation and multiple sclerosis: hot topics in the preservation of physical functioning. *Journal of the Neurological Sciences*, 311S1, S43–S47.
- Daniels, S. K. (2000). Swallowing apraxia: a disorder of the praxis system? *Dysphagia*, 15(3), 159–166. Springer.
- Daniels, S. K., Brailey, K., & Foundas, A. L. (1999). Lingual discoordination and dysphagia following acute stroke: analyses of lesion localization. *Dysphagia*, 14(2), 85–92.
- Daniels, S. K., & Foundas, A. L. (1997). The role of the insular cortex in dysphagia. *Dysphagia*, 12(3), 146–56.
- Daniels, S. K., & Foundas, A. L. (1999). Lesion localization in acute stroke patients with risk of aspiration. *Journal of Neuroimaging*, 9(2), 91–98.
- Daniels, S. K., & Huckabee, M. L. (2008). *Dysphagia following stroke*. San Diego, CA: Plural Publishing.
- Darling, W. G., Wolf, S. L., & Butler, A. J. (2006). Variability of motor potentials evoked by transcranial magnetic stimulation depends on muscle activation. *Experimental Brain Research*, 174(2), 376–385.
- Day, B. L., Dressler, D., Maertens de Noordhout, A., Marsden, C. D., Nakashima, K., Rothwell, J. C., & Thompson, P. D. (1989). Electric and magnetic stimulation of human motor cortex: surface EMG and single motor unit responses. *The Journal of Physiology*, 412, 449–473.

- Day, S. J., & Hulliger, M. (2001). Experimental simulation of cat electromyogram: evidence for algebraic summation of motor-unit action-potential trains. *Journal of Neurophysiology*, 86(5), 2144–2158.
- Dennis, M., Lewis, S., Cranswick, G., & Forbes, J. (2006). FOOD: a multicentre randomised trial evaluating feeding policies in patients admitted to hospital with a recent stroke. *Health Technology Assessment*, 10(2), iii–iv, ix–x, 1–120.
- Dennis, M. S., Lewis, S. C., & Warlow, C. (2005). Effect of timing and method of enteral tube feeding for dysphagic stroke patients (FOOD): a multicentre randomised controlled trial. *Lancet*, 365(9461), 764–72.
- Dobkin, B. H. (2005). Rehabilitation and functional neuroimaging dose-response trajectories for clinical trials. *Neurorehabilitation and Neural Repair*, 19(4), 276–282.
- Dodds, W. J., Hogan, W. J., Reid, D. P., Stewart, E. T., & Arndorfer, R. C. (1973). A comparison between primary esophageal peristalsis following wet and dry swallows. *Journal of Applied Physiology*, 35(6), 851–857.
- Dodds, W. J., Logemann, J. A., & Stewart, E. T. (1990). Radiologic assessment of abnormal oral and pharyngeal phases of swallowing. *American Journal of Roentgenology*, 154(5), 965–974.
- Dodds, W. J., Man, K. M., Cook, I. J., Kahrilas, P. J., Stewart, E. T., & Kern, M. K. (1988). Influence of bolus volume on swallow-induced hyoid movement in normal subjects. *American Journal of Roentgenology*, 150(6), 1307–1309.
- Dodds, W. J., Stewart, E. T., & Logemann, J. A. (1990). Physiology and radiology of the normal oral and pharyngeal phases of swallowing. *American Journal of Roentgenology*, 154(5), 953–963.
- Dodds, W. J., Taylor, A. J., Stewart, E. T., Kern, M. K., Logemann, J. A., & Cook, I. J. (1989). Tipper and dipper types of oral swallows. *American Journal of Roentgenology*, 153(6), 1197–1199.
- Doeltgen, S. H., Dalrymple-Alford, J., Ridding, M. C., & Huckabee, M. L. (2010). Differential effects of neuromuscular electrical stimulation parameters on submental motor-evoked potentials. *Neurorehabilitation and Neural Repair*, 24(6), 519–527.
- Doeltgen, S. H., Ridding, M. C., Dalrymple-Alford, J., & Huckabee, M. L. (2011). Task-dependent differences in corticobulbar excitability of the submental motor projections: Implications for neural control of swallowing. *Brain Research Bulletin*, 84(1), 88–93. Elsevier Inc.
- Doeltgen, S. H., Ridding, M. C., O’Beirne, G. A., Dalrymple-Alford, J., & Huckabee, M. L. (2009). Test-retest reliability of motor evoked potentials (MEPs) at the submental muscle group during volitional swallowing. *Journal of Neuroscience Methods*, 178(1), 134–137. Elsevier B.V.
- Doeltgen, S. H., Witte, U., Gumbley, F., & Huckabee, M. L. (2009). Evaluation of manometric measures during tongue-hold swallows. *American Journal of Speech-Language Pathology*, 18(1), 65–73.

- Donner, M. W., Bosma, J. F., & Robertson, D. L. (1985). Anatomy and physiology of the pharynx. *Gastrointestinal Radiology*, 10(3), 196–212.
- Donoghue, J. P. (1995). Plasticity of adult sensorimotor representations. *Current Opinion in Neurobiology*, 5(6), 749–754.
- Doty, R. W. (1968). Neural organization of deglutition, Alimentary Canal. In C. Code (Ed.), *Handbook of physiology* (2nd ed., pp. 1861–1902). Washington: American Physiological Society.
- Doty, R. W., & Bosma, J. F. (1956). An electromyographic analysis of reflex deglutition. *Journal of Neurophysiology*, 19(1), 44–60.
- Doty, R. W., Richmond, W. H., & Storey, A. T. (1967). Effect of medullary lesions on coordination of deglutition. *Experimental Neurology*, 17(1), 91–106.
- Duchateau, J., Semmler, J. G., & Enoka, R. M. (2006). Training adaptations in the behavior of human motor units. *Journal of Applied Physiology*, 101(6), 1766–1775.
- Duchêne, J., & Goubel, F. (1993). Surface electromyogram during voluntary contraction: processing tools and relation to physiological events. *Critical Reviews in Biomedical Engineering*, 21(4), 313–397.
- Duffy, J. R. (1995). *Motor speech disorders: Substrates, differential diagnosis, and management*. St Louis, MO: Mosby.
- D’Esposito, M., Zarahn, E., Aguirre, G. K., & Rypma, B. (1999). The effect of normal aging on the coupling of neural activity to the bold hemodynamic response. *NeuroImage*, 10(1), 6–14.
- Easterling, C., & Robbins, E. (2008). Dementia and dysphagia. *Geriatric Nursing*, 29(4), 275–285. Elsevier.
- Ekberg, O., Hamdy, S., Woisard, V., Wuttge-Hannig, A., & Ortega, P. (2002). Social and psychological burden of dysphagia: its impact on diagnosis and treatment. *Dysphagia*, 17(2), 139–146.
- Emshoff, R., Bertram, S., & Strobl, H. (1999). Ultrasonographic cross-sectional characteristics of muscles of the head and neck. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 87(1), 93–106. Elsevier.
- Enoka, R. M. (2008). *Neuromechanics of human movement* (4th Ed.). Champaign, IL: Human Kinetics.
- Enoka, R. M., Christou, E. a., Hunter, S. K., Kornatz, K. W., Semmler, J. G., Taylor, A. M., & Tracy, B. L. (2003). Mechanisms that contribute to differences in motor performance between young and old adults. *Journal of Electromyography and Kinesiology*, 13(1), 1–12.
- Epstein, C. M., Schwartzberg, D. G., Davey, K. R., & Sudderth, D. B. (1990). Localizing the site of magnetic brain stimulation in humans. *Neurology*, 40(4), 666–670.
- Ertekin, C. (2011). Voluntary versus spontaneous swallowing in man. *Dysphagia*, 26(2), 183–192.

- Ertekin, C., & Aydogdu, I. (2002). Electromyography of human cricopharyngeal muscle of the upper esophageal sphincter. *Muscle & Nerve*, 26(6), 729–739.
- Ertekin, C., & Aydogdu, I. (2003). Neurophysiology of swallowing. *Clinical Neurophysiology*, 114(12), 2226–2244.
- Ertekin, C., Aydogdu, I., Yüceyar, N., Pehlivan, M., Ertaş, M., Uludag, B., & Celebi, G. (1997). Effects of bolus volume on oropharyngeal swallowing: an electrophysiologic study in man. *The American Journal of Gastroenterology*, 92(11), 2049–2053.
- Ertekin, C., Pehlivan, M., Aydogdu, I., Ertaş, M., Uludag, B., Celebi, G., Colakoğlu, Z., et al. (1995). An electrophysiological investigation of deglutition in man. *Muscle & Nerve*, 18(10), 1177–1186.
- Eslick, G. D., & Talley, N. J. (2008). Dysphagia: epidemiology, risk factors and impact on quality of life--a population-based study. *Alimentary Pharmacology & Therapeutics*, 27(10), 971–979.
- Evans, W. J. (1995). What is sarcopenia? *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 50, 5–8.
- Evarts, E. V., Teräväinen, H., & Calne, D. B. (1981). Reaction time in Parkinson's disease. *Brain*, 104(Pt 1), 167–186.
- Falvo, M. J., Schilling, B. K., & Earhart, G. M. (2008). Parkinson's disease and resistive exercise: rationale, review, and recommendations. *Movement Disorders*, 23(1), 1–11.
- Farina, D., Merletti, R., & Enoka, R. M. (2004). The extraction of neural strategies from the surface EMG. *Journal of Applied Physiology*, 96(4), 1486–1495.
- Fathi, D., Ueki, Y., Mima, T., Koganemaru, S., Nagamine, T., Tawfik, A., & Fukuyama, H. (2010). Effects of aging on the human motor cortical plasticity studied by paired associative stimulation. *Clinical Neurophysiology*, 121(1), 90–93. International Federation of Clinical Neurophysiology.
- Faulkner, J. A., Larkin, L. M., Claflin, D. R., & Brooks, S. V. (2007). Age-related changes in the structure and function of skeletal muscles. *Clinical and Experimental Pharmacology & Physiology*, 34(11), 1091–1096.
- Feinberg, M. J., & Ekberg, O. (1991). Videofluoroscopy in elderly patients with aspiration: importance of evaluating both oral and pharyngeal stages of deglutition. *American Journal of Roentgenology*, 156(2), 293–296.
- Felix, V. N., Corrêa, S. M. A., & Soares, R. J. (2008). A therapeutic maneuver for oropharyngeal dysphagia in patients with parkinson's disease. *Clinics*, 63(5), 661–666.
- Fietzek, U. M., Heinen, F., Berweck, S., Maute, S., Hufschmidt, A., Schulte-Mönting, J., Lücking, C. H., et al. (2000). Development of the corticospinal system and hand motor function: central conduction times and motor performance tests. *Developmental Medicine and Child Neurology*, 42(4), 220–227.

- Finestone, H. M., Greene-Finestone, L. S., Wilson, E. S., & Teasell, R. W. (1996). Prolonged length of stay and reduced functional improvement rate in malnourished stroke rehabilitation patients. *Archives of Physical Medicine and Rehabilitation*, 77(4), 340–345.
- Finucane, T. E., & Bynum, J. P. (1996). Use of tube feeding to prevent aspiration pneumonia. *Lancet*, 348(9039), 1421–1424.
- Fischer, S. L., Belbeck, A. L., & Dickerson, C. R. (2010). The influence of providing feedback on force production and within-participant reproducibility during maximal voluntary exertions for the anterior deltoid, middle deltoid, and infraspinatus. *Journal of Electromyography and Kinesiology*, 20(1), 68–75.
- Fitch, W. T., & Giedd, J. (1999). Morphology and development of the human vocal tract: a study using magnetic resonance imaging. *The Journal of the Acoustical Society of America*, 106(3 Pt 1), 1511–1522.
- Fix, J. D. (2008). *Neuroanatomy* (4th Ed.). Baltimore: Lippincott Williams & Wilkins.
- Fling, B. W., Knight, C. a, & Kamen, G. (2009). Relationships between motor unit size and recruitment threshold in older adults: implications for size principle. *Experimental Brain Research*, 197(2), 125–133.
- Floyer-Lea, A., & Matthews, P. M. (2005). Distinguishable brain activation networks for short- and long-term motor skill learning. *Journal of Neurophysiology*, 94(1), 512–518.
- Folland, J. P., & Williams, A. G. (2007). The adaptations to strength training: morphological and neurological contributions to increased strength. *Sports Medicine*, 37(2), 145–168. Adis International.
- Foltys, H. (2003). Motor representation in patients rapidly recovering after stroke: a functional magnetic resonance imaging and transcranial magnetic stimulation study. *Clinical Neurophysiology*, 114(12), 2404–2415.
- Foltys, H., Kemeny, S., Krings, T., Boroojerdi, B., Sparing, R., Thron, A., & Töpper, R. (2000). The representation of the plegic hand in the motor cortex: a combined fMRI and TMS study. *Neuroreport*, 11(1), 147–150.
- Fontana, G., & Lavorini, F. (2006). Cough motor mechanisms. *Respiratory Physiology & Neurobiology*, 152(3), 266–281.
- Fox, P. T., Narayana, S., Tandon, N., Sandoval, H., Fox, S. P., Kochunov, P., & Lancaster, J. L. (2004). Column-based model of electric field excitation of cerebral cortex. *Human Brain Mapping*, 22(1), 1–14.
- Fraser, C. H., Power, M. L., Hamdy, S., Rothwell, J. C., Hobday, D., Hollander, I., Tyrell, P., et al. (2002). Driving plasticity in human adult motor cortex is associated with improved motor function after brain injury. *Neuron*, 34(5), 831–840.
- Fraser, C. H., Rothwell, J. C., Power, M. L., Hobson, A., Thompson, D. G., & Hamdy, S. (2003). Differential changes in human pharyngoesophageal motor excitability induced by swallowing, pharyngeal stimulation, and anesthesia. *American Journal of Physiology. Gastrointestinal and Liver Physiology*, 285(1), G137–144.

- Frattali, C. M., Sonies, B. C., Chi-Fishman, G., & Litvan, I. (1999). Effects of physostigmine on swallowing and oral motor functions in patients with progressive supranuclear palsy: A pilot study. *Dysphagia*, 14(3), 165–168.
- Friedman, L., Furberg, C., & DeMets, D. (2010). *Fundamentals of clinical trials* (4th ed.). New York: Springer Verlag.
- Fuh, J., Lee, R. C., Wang, S. J., Lin, C. H., Wang, P. N., Chiang, J. H., & Liu, H. C. (1997). Swallowing difficulty in Parkinson's disease. *Clinical Neurology and Neurosurgery*, 99(2), 106–112.
- Fujiu, M., & Logemann, J. A. (1996). Effect of a tongue-holding maneuver on posterior pharyngeal wall movement during deglutition. *American Journal of Speech-Language Pathology*, 5(1), 23–30. ASHA.
- Fujiyama, H., Garry, M. I., Levin, O., Swinnen, S. P., & Summers, J. J. (2009). Age-related differences in inhibitory processes during interlimb coordination. *Brain Research*, 1262, 38–47.
- Gabriel, D. A., Kamen, G., & Frost, G. (2006). Neural adaptations to resistive exercise: mechanisms and recommendations for training practices. *Sports Medicine*, 36(2), 133–149.
- Gallas, S., Marie, J. P., Leroi, a M., & Verin, E. (2009). Impact of swallowing and ventilation on oropharyngeal cortical representation. *Respiratory Physiology & Neurobiology*, 167(2), 208–213.
- Gandevia, S. C. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiological Reviews*, 81(4), 1725–1789.
- Garcia, J., Hakel, M., & Lazarus, C. L. (2004). Unexpected consequence of effortful swallowing: Case study report. *Journal of Medical Speech - Language Pathology*, 12(2), 59–66.
- Gay, T., Rendell, J. K., Spiro, J., Mosier, K. M., & Lurie, A. G. (1994). Coordination of oral cavity and laryngeal movements during swallowing. *Journal of Applied Physiology*, 77(1), 357–365.
- Georgiou, N., Iansek, R., Bradshaw, J. L., Phillips, J. G., Mattingley, J. B., & Bradshaw, J. A. (1993). An evaluation of the role of internal cues in the pathogenesis of parkinsonian hypokinesia. *Brain*, 116(6), 1575–1587.
- Gilbert, G. H., Heft, M. W., & Duncan, R. P. (1993). Mouth dryness as reported by older Floridians. *Community Dentistry and Oral Epidemiology*, 21(6), 390–397.
- Giusti, A., & Giambuzzi, M. (2008). Management of dysphagia in patients affected by multiple sclerosis: state of the art. *Neurological Sciences*, 29(4), S364–366.
- Glass, D. J. (2010). A critique of the hypothesis, and a defense of the question, as a framework for experimentation. *Clinical Chemistry*, 56(7), 1080–1085.
- Gleeson, D. (1999). Oropharyngeal swallowing and aging A review. *Journal of Communication Disorders*, 32(6), 373–396.

- Gonzalez Rothi, L. J., Musson, N., Rosenbek, J. C., & Sapienza, C. M. (2008). Neuroplasticity and rehabilitation research for speech, language, and swallowing disorders. *Journal of Speech, Language, and Hearing Research*, 51(1), S222–224.
- Gooden, B. R., Ridding, M. C., Miles, T. S., Nordstrom, M. A., & Thompson, P. D. (1999). Bilateral cortical control of the human anterior digastric muscles. *Experimental Brain Research*, 129(4), 582–591.
- Gordon, T., Thomas, C. K., Munson, J. B., & Stein, R. B. (2004). The resilience of the size principle in the organization of motor unit properties in normal and reinnervated adult skeletal muscles. *Canadian Journal of Physiology and Pharmacology*, 82(8-9), 645–661.
- Gow, D., Rothwell, J. C., Hobson, A., Thompson, D. G., & Hamdy, S. (2004). Induction of long-term plasticity in human swallowing motor cortex following repetitive cortical stimulation. *Clinical Neurophysiology*, 115(5), 1044–1051.
- Griffin, L., & Cafarelli, E. (2007). Transcranial magnetic stimulation during resistance training of the tibialis anterior muscle. *Journal of Electromyography and Kinesiology*, 17(4), 446–452.
- Guadagnoli, M. A., Leis, B., Van Gemmert, A. W. A., & Stelmach, G. E. (2002). The relationship between knowledge of results and motor learning in Parkinsonian patients. *Parkinsonism & Related Disorders*, 9(2), 89–95. Elsevier.
- Guggenmos, D. J., Barbay, S., Bethel-Brown, C., Nudo, R. J., & Stanford, J. A. (2009). Effects of tongue force training on orolingual motor cortical representation. *Behavioural Brain Research*, 201(1), 229–232. Elsevier.
- Gur, R. C., Mozley, P. D., Resnick, S. M., Gottlieb, G. L., Kohn, M., Zimmerman, R., Herman, G., et al. (1991). Gender differences in age effect on brain atrophy measured by magnetic resonance imaging. *Proceedings of the National Academy of Sciences of the United States of America*, 88(7), 2845–2849.
- Hallett, M. (2000). Transcranial magnetic stimulation and the human brain. *Nature*, 406(6792), 147–50. Nature Publishing Group.
- Hallett, M. (2007). Transcranial magnetic stimulation: a primer. *Neuron*, 55(2), 187–199. Elsevier.
- Hamdy, S., Aziz, Q., Rothwell, J. C., Crone, R., Hughes, D. G., Tallis, R. C. C., & Thompson, D. G. (1997). Explaining oropharyngeal dysphagia after unilateral hemispheric stroke. *The Lancet*, 350(9079), 686–692. Elsevier.
- Hamdy, S., Aziz, Q., Rothwell, J. C., Hobson, A., Barlow, J., & Thompson, D. G. (1997). Cranial nerve modulation of human cortical swallowing motor pathways. *The American journal of physiology*, 272(4 Pt 1), G802–8.
- Hamdy, S., Aziz, Q., Rothwell, J. C., Power, M. L., Singh, K. D., Nicholson, D. A., Tallis, R. C., et al. (1998). Recovery of swallowing after dysphagic stroke relates to functional reorganization in the intact motor cortex. *Gastroenterology*, 115(5), 1104–1112. Elsevier.
- Hamdy, S., Aziz, Q., Rothwell, J. C., Singh, K. D., Barlow, J., Hughes, D. G., Tallis, R. C., et al. (1996). The cortical topography of human swallowing musculature in health and disease. *Nature Medicine*, 2(11), 1217–1224. Nature Publishing Group.

- Hamdy, S., Jilani, S., Price, V., Parker, C., Hall, N., & Power, M. L. (2003). Modulation of human swallowing behaviour by thermal and chemical stimulation in health and after brain injury. *Neurogastroenterology and Motility*, 15(1), 69–77. Wiley Online Library.
- Hamdy, S., Mikulis, D. J., Crawley, A., Xue, S., Lau, H., Henry, S., & Diamant, N. E. (1999). Cortical activation during human volitional swallowing: an event-related fMRI study. *The American Journal of Physiology*, 277(1 Pt 1), G219–225.
- Hamdy, S., & Rothwell, J. C. (1998). Gut feelings about recovery after stroke: the organization and reorganization of human swallowing motor cortex. *Trends in Neurosciences*, 21(7), 278–282. Elsevier.
- Hamdy, S., Rothwell, J. C., Aziz, Q., Singh, K. D., & Thompson, D. G. (1998). Long-term reorganization of human motor cortex driven by short-term sensory stimulation. *Nature Neuroscience*, 1(1), 64–68. Nature Publishing Group.
- Hamdy, S., Rothwell, J. C., Brooks, D. J., Bailey, D., Aziz, Q., & Thompson, D. G. (1999). Identification of the cerebral loci processing human swallowing with H₂(15)O PET activation. *Journal of Neurophysiology*, 81(4), 1917–1926.
- Hamdy, S., Rothwell, J. C., Fraser, C. H., Power, M. L., Gow, D., & Thompson, D. G. (2002). Patterns of excitability in human esophageal sensorimotor cortex to painful and nonpainful visceral stimulation. *American Journal of Physiology. Gastrointestinal and Liver Physiology*, 282(2), G332–337.
- Hammond, G. (2002). Correlates of human handedness in primary motor cortex: a review and hypothesis. *Neuroscience and Biobehavioral Reviews*, 26(3), 285–292.
- Hanna-Pladdy, B., & Heilman, K. M. (2010). Dopaminergic modulation of the planning phase of skill acquisition in Parkinson's disease. *Neurocase*, 16(2), 182–190.
- Harridge, S. D., Kryger, A., & Stensgaard, A. (1999). Knee extensor strength, activation, and size in very elderly people following strength training. *Muscle & Nerve*, 22(7), 831–839.
- Harrington, D. L., & Haaland, K. Y. (1991). Sequencing in Parkinson's disease. Abnormalities in programming and controlling movement. *Brain*, 114(1), 99–115.
- Hartelius, L., & Svensson, P. (1994). Speech and swallowing symptoms associated with Parkinson's disease and multiple sclerosis: a survey. *Folia Phoniatrica et Logopaedica*, 46(1), 9–17.
- Heck, F. M., Doeltgen, S. H., & Huckabee, M. L. (2012). Effects of Submental Neuromuscular Electrical Stimulation on Pharyngeal Pressure Generation. *Archives of Physical Medicine and Rehabilitation*, xx, 1–8. the American Congress of Rehabilitation Medicine.
- Heemskerk, A.-W., & Roos, R. a C. (2011). Dysphagia in Huntington's disease: a review. *Dysphagia*, 26(1), 62–66.
- Heeneman, H., & Brown, D. H. (1986). Senescent changes in and about the oral cavity and pharynx. *The Journal of Otolaryngology*, 15(4), 214–216.
- Heggie, J. C., Liddell, N. A., & Maher, K. P. (2001). *Applied imaging technology* (4th ed.). Melbourne: St Vincent's Hospital.

- Heijnen, B. J., Speyer, R., Baijens, L. W. J., & Bogaardt, H. C. a. (2012). Neuromuscular electrical stimulation versus traditional therapy in patients with Parkinson's disease and oropharyngeal Dysphagia: effects on quality of life. *Dysphagia*, 27(3), 336–345.
- Hermanowicz, N. (2007). Cranial Nerves IX (Glossopharyngeal) and X (Vagus). In C. G. Goetz (Ed.), *Textbook of Clinical Neurology* (3rd Ed., pp. 217–229). Philadelphia, PA: Elsevier Inc.
- Hiiemae, K. M., & Palmer, J. B. (1999). Food transport and bolus formation during complete feeding sequences on foods of different initial consistency. *Dysphagia*, 14(1), 31–42.
- Hind, J. A., Nicosia, M. A., Roecker, E. B., Carnes, M. L., & Robbins, J. A. (2001). Comparison of effortful and noneffortful swallows in healthy middle-aged and older adults. *Archives of Physical Medicine and Rehabilitation*, 82(12), 1661–1665. Elsevier.
- Hinder, M. R., Schmidt, M. W., Garry, M. I., & Summers, J. J. (2010). The effect of ballistic thumb contractions on the excitability of the ipsilateral motor cortex. *Experimental Brain Research*, 201(2), 229–238.
- Hirano, M., Kuroiwa, Y., Tanaka, S., Matsuoka, H., Sato, K., & Yoshida, T. (1992). Dysphagia following various degrees of surgical resection for oral cancer. *The Annals of Otology, Rhinology & Laryngology*, 101(2 Pt 1), 138–141.
- Hiraoka, K. (2004). Movement-related cortical potentials associated with saliva and water bolus swallowing. *Dysphagia*, 19(3), 155–159.
- Hiss, S. G., & Huckabee, M. L. (2005). Timing of pharyngeal and upper esophageal sphincter pressures as a function of normal and effortful swallowing in young healthy adults. *Dysphagia*, 20(2), 149–156.
- Hoehn, M., & Yahr, M. D. (1967). Parkinsonism: onset, progression and mortality. *Neurology*, 17(5), 427–442.
- Hoffman, M. R., Ciucci, M. R., Mielens, J. D., Jiang, J. J., & McCulloch, T. M. (2010). Pharyngeal swallow adaptations to bolus volume measured with high-resolution manometry. *The Laryngoscope*, 120(12), 2367–73.
- Hoffman, M. R., Mielens, J. D., Ciucci, M. R., Jones, C. a, Jiang, J. J., & McCulloch, T. M. (2012). High-resolution manometry of pharyngeal swallow pressure events associated with effortful swallow and the Mendelsohn maneuver. *Dysphagia*, 27(3), 418–26.
- Hogrel, J. (2003). Use of surface EMG for studying motor unit recruitment during isometric linear force ramp. *Journal of Electromyography and Kinesiology*, 13(5), 417–423.
- Horner, J., Alberts, M. J., Dawson, D. V., & Cook, G. M. (1994). Swallowing in Alzheimer's disease. *Alzheimer disease and associated disorders*, 8(3), 177–89.
- Horner, J., Massey, E. W., Riski, J. E., Lathrop, D. L., & Chase, K. N. (1988). Aspiration following stroke: clinical correlates and outcome. *Neurology*, 38(9), 1359–1362.
- Hubal, M. J., Gordish-Dressman, H., Thompson, P. D., Price, T. B., Hoffman, E. P., Angelopoulos, T. J., Gordon, P. M., et al. (2005). Variability in muscle size and strength

- gain after unilateral resistance training. *Medicine and Science in Sports and Exercise*, 37(6), 964–972.
- Huckabee, M. L., Butler, S. G., Barclay, M., & Jit, S. (2005). Submental surface electromyographic measurement and pharyngeal pressures during normal and effortful swallowing. *Archives of Physical Medicine and Rehabilitation*, 86(11), 2144–2149.
- Huckabee, M. L., & Cannito, M. P. (1999). Outcomes of Swallowing Rehabilitation in Chronic Brainstem Dysphagia: A Retrospective Evaluation. *Dysphagia*, 14(2), 93–109.
- Huckabee, M. L., Deecke, L., Cannito, M. P., Gould, H. J., & Mayr, W. (2003). Cortical control mechanisms in volitional swallowing: the Bereitschaftspotential. *Brain Topography*, 16(1), 3–17.
- Huckabee, M. L., Low, I. S., & McAuliffe, M. J. (2012). Variability in clinical surface electromyography recording of submental muscle activity in swallowing of healthy participants. *Asia Pacific Journal of Speech, Language, and Hearing*, 15(3), 175–186.
- Huckabee, M. L., & Steele, C. M. (2006). An analysis of lingual contribution to submental surface electromyographic measures and pharyngeal pressure during effortful swallow. *Archives of physical medicine and rehabilitation*, 87(8), 1067–72.
- Hueber, T., Benaroya, E.-L., Chollet, G., Denby, B., Dreyfus, G., & Stone, M. (2010). Development of a silent speech interface driven by ultrasound and optical images of the tongue and lips. *Speech Communication*, 52(4), 288–300.
- Hughes, T. A., & Wiles, C. M. (1996). Clinical measurement of swallowing in health and in neurogenic dysphagia. *QJM*, 89(2), 109–116.
- Hula, Austermann, N. S., Robin, D. A., Maas, E., Ballard, K. J., & Schmidt, R. A. (2008). Effects of feedback frequency and timing on acquisition, retention, and transfer of speech skills in acquired apraxia of speech. *Journal of Speech, Language, and Hearing Research*, 51(5), 1088–1113.
- Humbert, I. A., Fitzgerald, M. E., McLaren, D. G., Johnson, S., Porcaro, E., Kosmatka, K., Hind, J. A., et al. (2009). Neurophysiology of swallowing: effects of age and bolus type. *NeuroImage*, 44(3), 982–091. Elsevier Inc.
- Humbert, I. A., & Robbins, J. A. (2008). Dysphagia in the elderly. *Physical medicine and rehabilitation clinics of North America*, 19(4), 853–66, ix–x.
- Hutchinson, S. (2002). Age-related differences in movement representation. *NeuroImage*, 17(4), 1720–1728.
- Häkkinen, K., & Komi, P. V. (1983). Electromyographic changes during strength training and detraining. *Medicine and Science in Sports and Exercise*, 15(6), 455–460.
- Häkkinen, K., Newton, R. U., Gordon, S. E., McCormick, M., Volek, J. S., Nindl, B. C., Gotshalk, L. A., et al. (1998). Changes in muscle morphology, electromyographic activity, and force production characteristics during progressive strength training in young and older men. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 53(6), B415–423.

- Ito, M. (2002). Historical review of the significance of the cerebellum and the role of Purkinje cells in motor learning. *Annals of the New York Academy of Sciences*, 978, 273–288.
- Jacob, P., Kahrilas, P. J., Logemann, J. A., Shah, V., & Ha, T. (1989). Upper esophageal sphincter opening and modulation during swallowing. *Gastroenterology*, 97(6), 1469–1478.
- Jafari, S., Prince, R. A., Kim, D. Y., & Paydarfar, D. (2003). Sensory regulation of swallowing and airway protection: a role for the internal superior laryngeal nerve in humans. *The Journal of Physiology*, 550(1), 287–304.
- Jain, P. (2008). High-resolution sonography of sublingual space. *Journal of Medical Imaging and Radiation Oncology*, 52(2), 101–108.
- Jayasekeran, V., Rothwell, J. C., & Hamdy, S. (2011). Non-invasive magnetic stimulation of the human cerebellum facilitates cortico-bulbar projections in the swallowing motor system. *Neurogastroenterology and Motility*, 23(9), 831–341.
- Jean, A. (1984). Brainstem organization of the swallowing network. *Brain, Behavior and Evolution*, 25(2-3), 109–116. Karger Publishers.
- Jean, A. (2001). Brain stem control of swallowing: neuronal network and cellular mechanisms. *Physiological Reviews*, 81(2), 929–969.
- Jean, A., Amri, M., & Calas, A. (1983). Connections between the ventral medullary swallowing area and the trigeminal motor nucleus of the sheep studied by tracing techniques. *Journal of the Autonomic Nervous System*, 7(2), 87–96.
- Jean, A., & Car, A. (1979). Inputs to the swallowing medullary neurons from the peripheral afferent fibers and the swallowing cortical area. *Brain research*, 178(2-3), 567.
- Jensen, J. L., Marstrand, P. C. D., & Nielsen, J. B. (2005). Motor skill training and strength training are associated with different plastic changes in the central nervous system. *Journal of Applied Physiology*, 99(4), 1558–1568.
- Johnson, I. P., & Duberley, R. M. (1998). Motoneuron survival and expression of neuropeptides and neurotrophic factor receptors following axotomy in adult and ageing rats. *Neuroscience*, 84(1), 141–150.
- Johnston, B. T., Li, Q., Castell, J. A., & Castell, D. O. (1995). Swallowing and esophageal function in Parkinson's disease. *The American Journal of Gastroenterology*, 90(10), 1741–1746.
- Kagel, M. C., & Leopold, N. A. (1992). Dysphagia in Huntington's disease: a 16-year retrospective. *Dysphagia*, 7(2), 106–114.
- Kahrilas, P. J. (1993). Pharyngeal structure and function. *Dysphagia*, 8(4), 303–307.
- Kahrilas, P. J. (1997). Anatomy and physiology of the gastroesophageal junction. *Gastroenterology Clinics of North America*, 26(3), 467–486.
- Kahrilas, P. J., Dodds, W. J., Dent, J., Logemann, J. A., & Shaker, R. (1988). Upper esophageal sphincter function during deglutition. *Gastroenterology*, 95(1), 52–62.

- Kahrilas, P. J., Lin, S., Logemann, J. A., Ergun, G. A., & Facchini, F. (1993). Deglutitive tongue action: volume accommodation and bolus propulsion. *Gastroenterology*, 104(1), 152–162.
- Kahrilas, P. J., & Logemann, J. A. (1993). Volume accommodation during swallowing. *Dysphagia*, 8(3), 259–265.
- Kahrilas, P. J., Logemann, J. A., Krugler, C., & Flanagan, E. (1991). Volitional augmentation of upper esophageal sphincter opening during swallowing. *The American Journal of Physiology*, 260(3 Pt 1), G450–456.
- Kahrilas, P. J., Logemann, J. A., Lin, S., & Ergun, G. A. (1992). Pharyngeal clearance during swallowing: a combined manometric and videofluoroscopic study. *Gastroenterology*, 103(1), 128–136.
- Kalf, J. G., de Swart, B. J. M., Bloem, B. R., & Munneke, M. (2012). Prevalence of oropharyngeal dysphagia in Parkinson's disease: a meta-analysis. *Parkinsonism & Related Disorders*, 18(4), 311–5.
- Kalia, M. (2003). Dysphagia and aspiration pneumonia in patients with Alzheimer's disease. *Metabolism: Clinical and Experimental*, 52(10), 36–38.
- Kamen, G. (2005). Aging, resistance training, and motor unit discharge behavior. *Canadian Journal of Applied Physiology*, 30(3), 341–351.
- Kamen, G., & Gabriel, D. (2010). *Essentials of electromyography*. Champaign, IL: Human Kinetics.
- Kamen, G., & Knight, C. A. (2004). Training-related adaptations in motor unit discharge rate in young and older adults. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 59(12), 1334–1338.
- Kang, S. H., Kim, D.-K., Seo, K.-M., & Seo, J.-H. (2011). Usefulness of videofluoroscopic swallow study with mixed consistency food for patients with stroke or other brain injuries. *Journal of Korean Medical Science*, 26(3), 425–430.
- Kapogiannis, D., & Wassermann, E. M. (2008). Transcranial magnetic stimulation in Clinical Pharmacology. *Central Nervous System Agents in Medicinal Chemistry*, 8(4), 234–240.
- Karni, A., Meyer, G., Jezzard, P., Adams, M. M., Turner, R., & Ungerleider, L. G. (1995). Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature*, 377(6545), 155–158.
- Karni, A., Meyer, G., Rey-Hipolito, C., Jezzard, P., Adams, M. M., Turner, R., & Ungerleider, L. G. (1998). The acquisition of skilled motor performance: fast and slow experience-driven changes in primary motor cortex. *Proceedings of the National Academy of Sciences of the United States of America*, 95(3), 861–868.
- Karni, A., & Sagi, D. (1993). The time course of learning a visual skill. *Nature*, 365(6443), 250–252.
- Kashiwagi, K., Tanaka, M., Kawazoe, T., Furuichi, K., & Takada, H. (1995). Effect of amplitude normalization on surface EMG linear envelopes of masticatory muscles during gum chewing. *Journal of Osaka Dental University*, 29(1), 19–28.

- Kaur, G., English, C., & Hillier, S. (2012). How physically active are people with stroke in physiotherapy sessions aimed at improving motor function? A systematic review. *Stroke Research and Treatment*, 1–9.
- Keel, J. C., Smith, M. J., & Wassermann, E. M. (2001). A safety screening questionnaire for transcranial magnetic stimulation. *Clinical Neurophysiology*, 112(4), 720.
- Keenan, K. G., Farina, D., Merletti, R., & Enoka, R. M. (2006). Influence of motor unit properties on the size of the simulated evoked surface EMG potential. *Experimental Brain Research*, 169(1), 37–49.
- Kelly, C., Foxe, J. J., & Garavan, H. (2006). Patterns of normal human brain plasticity after practice and their implications for neurorehabilitation. *Archives of Physical Medicine and Rehabilitation*, 87(12), S20–29.
- Kendall, K. A., McKenzie, S., Leonard, R. J., Gonçalves, M. I., & Walker, A. (2000). Timing of events in normal swallowing: a videofluoroscopic study. *Dysphagia*, 15(2), 74–83.
- Kent, R. D. (2004). The uniqueness of speech among motor systems. *Clinical Linguistics & Phonetics*, 18(6-8), 495–505.
- Kern, M. K., Birn, R., Jaradeh, S., Jesmanowicz, A., Cox, R. W., Hyde, J., & Shaker, R. (2001). Swallow-related cerebral cortical activity maps are not specific to deglutition. *American Journal of Physiology. Gastrointestinal and Liver Physiology*, 280(4), G531–538.
- Kern, M. K., Birn, R. M., Jaradeh, S., Jesmanowicz, A., Cox, R. W., Hyde, J. S., & Shaker, R. (1998). Identification and characterization of cerebral cortical response to esophageal mucosal acid exposure and distention. *Gastroenterology*, 115(6), 1353–1362.
- Kern, M. K., Jaradeh, S., Arndorfer, R. C., & Shaker, R. (2001). Cerebral cortical representation of reflexive and volitional swallowing in humans. *American Journal of Physiology. Gastrointestinal and Liver Physiology*, 280(3), G354–360.
- Kessler, J. P., & Jean, A. (1985). Identification of the medullary swallowing regions in the rat. *Experimental Brain Research*, 57(2), 256–263.
- Kidgell, D. J., & Pearce, A. J. (2010). Corticospinal properties following short-term strength training of an intrinsic hand muscle. *Human Movement Science*, 29(5), 631–641. Elsevier B.V.
- Kidgell, D. J., & Pearce, A. J. (2011). What has transcranial magnetic stimulation taught us about neural adaptations to strength training? A brief review. *Journal of Strength and Conditioning Research*, 25(11), 3208–3217.
- Kidgell, D. J., Stokes, M. A., & Pearce, A. J. (2011). Strength training of one limb increases corticomotor excitability projecting to the contralateral homologous limb. *Motor Control*, 15(2), 247–266.
- Kiers, L., Cros, D., Chiappa, K. H., & Fang, J. (1993). Variability of motor potentials evoked by transcranial magnetic stimulation. *Electroencephalography and Clinical Neurophysiology*, 89(6), 415–423.

- Kikuchi, T. (1970). A contribution to the morphology of the ansa cervicalis and the phrenic nerve. *Kaibogaku Zasshi*, 45(5), 242–281.
- Kim, J., Davenport, P., & Sapienza, C. (2009). Effect of expiratory muscle strength training on elderly cough function. *Archives of gerontology and geriatrics*, 48(3), 361–6.
- Kisner, C., & Colby, L. (2007). *Therapeutic exercise: Foundations and techniques* (5th Ed.). Philadelphia, PA: F.A. Davis Company.
- Kleim, J. A., Barbay, S., Cooper, N. R., Hogg, T. M., Reidel, C. N., Remple, M. S., & Nudo, R. J. (2002). Motor learning-dependent synaptogenesis is localized to functionally reorganized motor cortex. *Neurobiology of Learning and Memory*, 77(1), 63–77.
- Kleim, J. A., Chan, S., Pringle, E., Schallert, K., Procaccio, V., Jimenez, R., & Cramer, S. C. (2006). BDNF val66met polymorphism is associated with modified experience-dependent plasticity in human motor cortex. *Nature Neuroscience*, 9(6), 735–737.
- Kleim, J. A., Lussnig, E., Schwarz, E. R., Comery, T. A., & Greenough, W. T. (1996). Synaptogenesis and Fos expression in the motor cortex of the adult rat after motor skill learning. *The Journal of Neuroscience*, 16(14), 4529–4535.
- Kleim, J. A., Swain, R. A., Armstrong, K. A., Napper, R. M., Jones, T. A., & Greenough, W. T. (1998). Selective synaptic plasticity within the cerebellar cortex following complex motor skill learning. *Neurobiology of Learning and Memory*, 69(3), 274–289.
- Klem, G. H., Lüders, H. O., Jasper, H. H., & Elger, C. (1999). The ten-twenty electrode system of the International Federation. The International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology*, 52, 3–6.
- Klintsova, A. Y., Dickson, E., Yoshida, R., & Greenough, W. T. (2004). Altered expression of BDNF and its high-affinity receptor TrkB in response to complex motor learning and moderate exercise. *Brain Research*, 1028(1), 92–104.
- Komi, P. V. (1986). Training of muscle strength and power: interaction of neuromotoric, hypertrophic, and mechanical factors. *International Journal of Sports Medicine*, 7(1), 10–15.
- Komisaruk, B. R., Mosier, K. M., Liu, W. C., Criminale, C., Zaborszky, L., Whipple, B., & Kalnin, A. (2002). Functional localization of brainstem and cervical spinal cord nuclei in humans with fMRI. *American Journal of Neuroradiology*, 23(4), 609–617.
- Korfage, J. A. ., Koolstra, J., Langenbach, G., & van Eijden, T. M. G. J. (2005). Fiber-type composition of the human jaw muscles (part 2) role of hybrid fibers and factors responsible for inter-individual variation. *Journal of Dental Research*, 84(9), 784–793. SAGE Publications.
- Koski, L., Mernar, T. J., & Dobkin, B. H. (2004). Immediate and long-term changes in corticomotor output in response to rehabilitation: correlation with functional improvements in chronic stroke. *Neurorehabilitation and neural repair*, 18(4), 230–249.
- Kothari, M., Svensson, P., Huo, X., Ghovanloo, M., & Baad-Hansen, L. (2012). Force and complexity of tongue task training influences behavioral measures of motor learning. *European Journal of Oral Sciences*, 120(1), 46–53.

- Kraemer, W. J., & Newton, R. U. (2000). Training for muscular power. *Physical Medicine and Rehabilitation Clinics of North America*, 11(2), 341–368, vii.
- Krakauer, J. W., Carmichael, S. T., Corbett, D., & Wittenberg, G. F. (2012). Getting neurorehabilitation right: what can be learned from animal models? *Neurorehabilitation and Neural Repair*, 26(8), 923–31.
- Krings, T., Buchbinder, B. R., Butler, W. E., Chiappa, K. H., Jiang, H. J., Cosgrove, R. G., & Rosen, B. R. (1997). Functional magnetic resonance imaging and transcranial magnetic stimulation: complementary approaches in the evaluation of cortical motor function. *Neurology*, 48(5), 1406–1416.
- Kruger, E., Teasell, R. W., Salter, K., Foley, N., & Hellings, C. (2007). The rehabilitation of patients recovering from brainstem strokes: case studies and clinical considerations. *Topics in Stroke Rehabilitation*, 14(5), 56–64.
- Kubo, K., Kanehisa, H., & Fukunaga, T. (2001). Effects of different duration isometric contractions on tendon elasticity in human quadriceps muscles. *The Journal of Physiology*, 536(Pt 2), 649–655.
- Kuhl, V., Eicke, B. M., Dieterich, M., & Urban, P. P. (2003). Sonographic analysis of laryngeal elevation during swallowing. *Journal of Neurology*, 250(3), 333–337. Springer.
- Kuhlemeier, K. V. (1994). Epidemiology and dysphagia. *Dysphagia*, 9(4), 209–217.
- Kuhlemeier, K. V., & Stiens, S. A. (1994). Racial disparities in severity of cerebrovascular events. *Stroke*, 25(11), 2126–2131.
- Kuiken, T. A., Amir, H., & Scheidt, R. A. (2004). Computerized biofeedback knee goniometer: acceptance and effect on exercise behavior in post-total knee arthroplasty rehabilitation. *Archives of Physical Medicine and Rehabilitation*, 85(6), 1026–1030.
- Kuramoto, H., Kawano, H., Sakamoto, H., & Furness, J. B. (1999). Motor innervation by enteric nerve fibers containing both nitric oxide synthase and galanin immunoreactivities in the striated muscle of the rat esophagus. *Cell and Tissue Research*, 295(2), 241–245.
- Kwakkel, G. (2006). Impact of intensity of practice after stroke: issues for consideration. *Disability and Rehabilitation*, 28(13-14), 823–830.
- Kwakkel, G., Wagenaar, R. C., Twisk, J. W., Lankhorst, G. J., & Koetsier, J. C. (1999). Intensity of leg and arm training after primary middle-cerebral-artery stroke: a randomised trial. *Lancet*, 354(9174), 191–196.
- Kwiatek, M. A., Mirza, F., Kahrilas, P. J., & Pandolfino, J. E. (2009). Hyperdynamic upper esophageal sphincter pressure: a manometric observation in patients reporting globus sensation. *The American Journal of Gastroenterology*, 104(2), 289–298.
- Langan, J., Peltier, S. J., Bo, J., Fling, B. W., Welsh, R. C., & Seidler, R. D. (2010). Functional implications of age differences in motor system connectivity. *Frontiers in Systems Neuroscience*, 4, 1–11.

- Langdon, P. C., Lee, A. H., & Binns, C. W. (2007). Dysphagia in acute ischaemic stroke: severity, recovery and relationship to stroke subtype. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia*, 14(7), 630–4.
- Langmore, S. E., Terpenning, M. S., Schork, A., Chen, Y., Murray, J. T., Lopatin, D., & Loesche, W. J. (1998). Predictors of aspiration pneumonia: how important is dysphagia? *Dysphagia*, 13(2), 69–81.
- de Lateur, B. J. (1996). Therapeutic exercise. In R. L. Braddom (Ed.), *Physical medicine and rehabilitation* (pp. 401–419). Philadelphia, PA: W. B. Saunders.
- Lazarus, C. L., Logemann, J. A., Huang, C.-F., & Rademaker, A. W. (2003). Effects of two types of tongue strengthening exercises in young normals. *Folia Phoniatrica et Logopaedica*, 55(4), 199–205.
- Lazarus, C. L., Logemann, J. A., Pauloski, B. R., Colangelo, L. A., Kahrilas, P. J., Mittal, B. B., & Pierce, M. (1996). Swallowing disorders in head and neck cancer patients treated with radiotherapy and adjuvant chemotherapy. *The Laryngoscope*, 106(9 Pt 1), 1157–1166.
- Lazarus, C. L., Logemann, J. A., Song, C. W., Rademaker, A. W., & Kahrilas, P. J. (2002). Effects of voluntary maneuvers on tongue base function for swallowing. *Folia Phoniatrica et Logopaedica*, 54(4), 171–176.
- Leek, M. R. (2001). Adaptive procedures in psychophysical research. *Attention, Perception, & Psychophysics*, 63(8), 1279–1292. Springer.
- Lemmer, J. T., Hurlbut, D. E., Martel, G. F., Tracy, B. L., Ivey, F. M., Metter, E. J., Fozard, J. L., et al. (2000). Age and gender responses to strength training and detraining. *Medicine and Science in Sports and Exercise*, 32(8), 1505–1512.
- Lenius, K., Carnaby-Mann, G. D., & Crary, M. A. (2009). The relationship between lingual-palatal pressures and submental surface electromyographic signals. *Journal of Oral Rehabilitation*, 36(2), 118–123.
- Leonard, R. J., Kendall, K. A., McKenzie, S., Gonçalves, M. I., & Walker, A. (2000). Structural displacements in normal swallowing: a videofluoroscopic study. *Dysphagia*, 15(3), 146–152.
- Leonard, R. J., & McKenzie, S. (2006). Hyoid-bolus transit latencies in normal swallow. *Dysphagia*, 21(3), 183–190.
- Leong, B., Kamen, G., Patten, C., & Burke, J. R. (1999). Maximal motor unit discharge rates in the quadriceps muscles of older weight lifters. *Medicine and Science in Sports and Exercise*, 31(11), 1638–1644.
- Leopold, N. A., & Kagel, M. C. (1997). Pharyngo-esophageal dysphagia in Parkinson's disease. *Dysphagia*, 12(1), 11–18. Springer.
- Lever, T. E., Cox, K. T., Holbert, D., Shahrier, M., Hough, M., & Kelley-Salamon, K. (2007). The effect of an effortful swallow on the normal adult esophagus. *Dysphagia*, 22(4), 312–325.

- Levitt, H. (1971). Transformed up-down methods in psychoacoustics. *The Journal of the Acoustical Society of America*, 49(2), 467.
- Lexell, J. (1995). Human aging, muscle mass, and fiber type composition. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 50, 11–16.
- Liepert, J., Bauder, H., Wolfgang, H. R., Miltner, W. H. R., Taub, E., & Weiller, C. (2000). Treatment-induced cortical reorganization after stroke in humans. *Stroke*, 31(6), 1210–1216.
- Liepert, J., Dettmers, C., Terborg, C., & Weiller, C. (2001). Inhibition of ipsilateral motor cortex during phasic generation of low force. *Clinical Neurophysiology*, 112(1), 114–121.
- Liepert, J., Graef, S., Uhde, I., Leidner, O., & Weiller, C. (2000). Training-induced changes of motor cortex representations in stroke patients. *Acta Neurologica Scandinavica*, 101(5), 321–326.
- Ling, S. M., Conwit, R. a, Ferrucci, L., & Metter, E. J. (2009). Age-associated changes in motor unit physiology: observations from the Baltimore Longitudinal Study of Aging. *Archives of Physical Medicine and Rehabilitation*, 90(7), 1237–1240. the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation.
- Livingston, S. C., Goodkin, H. P., & Ingersoll, C. D. (2010). The influence of gender, hand dominance, and upper extremity length on motor evoked potentials. *Journal of Clinical Monitoring and Computing*, 24(6), 427–436.
- Lof, G. L., & Robbins, J. A. (1990). Test-retest variability in normal swallowing. *Dysphagia*, 4(4), 236–242.
- Logemann, J. A. (1988). Swallowing physiology and pathophysiology. *Otolaryngologic Clinics of North America*, 21(4), 613–623.
- Logemann, J. A. (1990). Effects of aging on the swallowing mechanism. *Otolaryngologic cClinics of North America*, 23(6), 1045–1056.
- Logemann, J. A. (1998). *Evaluation and treatment of swallowing disorders* (2nd ed.). Austin, TX: ProEd.
- Logemann, J. A. (2005). The role of exercise programs for dysphagia patients. *Dysphagia*, 20(2), 139–140.
- Logemann, J. A., & Kahrilas, P. J. (1990). Relearning to swallow after stroke-application of maneuvers and indirect biofeedback: a case study. *Neurology*, 40(7), 1136–1138.
- Logemann, J. A., Pauloski, B. R., Rademaker, A. W., Colangelo, L. A., Kahrilas, P. J., & Smith, C. H. (2000). Temporal and biomechanical characteristics of oropharyngeal swallow in younger and older men. *Journal of Speech, Language, and Hearing Research*, 43(5), 1264–1274.
- Logemann, J. A., Rademaker, A., Pauloski, B. R., Kelly, A., Stangl-McBreen, C., Antinoja, J., Grande, B., et al. (2009). A randomized study comparing the Shaker exercise with traditional therapy: a preliminary study. *Dysphagia*, 24(4), 403–411.

- Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature*, 412(6843), 150–157.
- Lorefält, B., Ganowiak, W., Pålhagen, S., Toss, G., Unosson, M., & Granérus, A.-K. (2004). Factors of importance for weight loss in elderly patients with Parkinson's disease. *Acta Neurologica Scandinavica*, 110(3), 180–187.
- Lorish, T. R., Sandin, K. J., Roth, E. J., & Noll, S. F. (1994). Stroke rehabilitation. 3. Rehabilitation evaluation and management. *Archives of Physical Medicine and Rehabilitation*, 75(5), S47–51.
- Lotze, M., Kaethner, R., Erb, M., Cohen, L. G., Grodd, W., & Topka, H. (2003). Comparison of representational maps using functional magnetic resonance imaging and transcranial magnetic stimulation. *Clinical Neurophysiology*, 114(2), 306–312. Elsevier.
- Loukas, M., Thorsell, A., Tubbs, R. S., Kapos, T., Louis, R. G., Vulis, M., Hage, R., et al. (2007). The ansa cervicalis revisited. *Folia Morphologica*, 66(2), 120–125.
- Lowell, S. Y., Poletto, C. J., Knorr-Chung, B. R., Reynolds, R. C., Simonyan, K., & Ludlow, C. L. (2008). Sensory stimulation activates both motor and sensory components of the swallowing system. *NeuroImage*, 42(1), 285–295.
- De Luca, C. J. (1997). The Use of surface electromyography in biomechanics. *Journal of Applied Biomechanics*, 13(2), 135–163.
- Ludlow, C. L., Hoit, J., Kent, R., Ramig, L., Shrivastav, R., Strand, E., Yorkston, K., et al. (2008). Translating principles of neural plasticity into research on speech motor control recovery and rehabilitation. *Journal of Speech, Language, and Hearing Research*, 51(1), S240–258. ASHA.
- van Lunteren, E., Vafaie, H., & Salomone, R. J. (1995). Comparative effects of aging on pharyngeal and diaphragm muscles. *Respiration Physiology*, 99(1), 113–125.
- Luschei, E. (1991). Development of objective standards of nonspeech oral strength and performance: An advocate's views. In C. A. Moore, K. M. Yorkston, & D. R. Beukelman (Eds.), *Dysarthria and apraxia of speech: Perspective on management* (pp. 3–13). Baltimore: Paul H. Brookes.
- Léonard, G., & Tremblay, F. (2007). Corticomotor facilitation associated with observation, imagery and imitation of hand actions: a comparative study in young and old adults. *Experimental Brain Research*, 177(2), 167–175.
- Maccabee, P. J., Amassian, V. E., Eberle, L. P., & Cracco, R. Q. (1993). Magnetic coil stimulation of straight and bent amphibian and mammalian peripheral nerve in vitro: locus of excitation. *The Journal of Physiology*, 460, 201–219.
- Macrae, P. (2011). *Biomechanical and neurophysiological changes associated with modified head-lift and effortful-swallowing rehailitation techniques*. Doctoral dissertation, University of Canterbury, New Zealand.

- Macrae, P., Doeltgen, S. H., Jones, R. D., & Huckabee, M. L. (2012). Intra- and inter-rater reliability for analysis of hyoid displacement measured with sonography. *Journal of Clinical Ultrasound*, 40(2), 74–78.
- Maeda, F., Keenan, J. P., Tormos, J. M., Topka, H., & Pascual-Leone, A. (2000). Modulation of corticospinal excitability by repetitive transcranial magnetic stimulation. *Clinical Neurophysiology*, 111(5), 800–805.
- Malandraki, G. a, Perlman, A. L., Karampinos, D. C., & Sutton, B. P. (2011). Reduced somatosensory activations in swallowing with age. *Human Brain Mapping*, 32(5), 730–743.
- Malandraki, G. a, Sutton, B. P., Perlman, A. L., & Karampinos, D. C. (2010). Age-related differences in laterality of cortical activations in swallowing. *Dysphagia*, 25(3), 238–249.
- Malandraki, G. a, Sutton, B. P., Perlman, A. L., Karampinos, D. C., & Conway, C. (2009). Neural activation of swallowing and swallowing-related tasks in healthy young adults: an attempt to separate the components of deglutition. *Human Brain Mapping*, 30(10), 3209–3226.
- Mann, G. D. C., Hankey, G. J., & Cameron, D. (1999). Swallowing function after stroke: prognosis and prognostic factors at 6 months. *Stroke*, 30(4), 744–748.
- Manor, Y., Balas, M., Giladi, N., Mootanah, R., & Cohen, J. T. (2009). Anxiety, depression and swallowing disorders in patients with Parkinson's disease. *Parkinsonism & Related Disorders*, 15(6), 453–456.
- Marik, P. E., & Kaplan, D. (2003). Aspiration pneumonia and dysphagia in the elderly. *Chest*, 124(1), 328–336.
- Martin, R. E., Barr, A., MacIntosh, B., Smith, R. C., Stevens, T., Taves, D., Gati, J., et al. (2007). Cerebral cortical processing of swallowing in older adults. *Experimental Brain research*, 176(1), 12–22.
- Martin, R. E., Goodyear, B. G., Gati, J. S., & Menon, R. S. (2001). Cerebral cortical representation of automatic and volitional swallowing in humans. *Journal of Neurophysiology*, 85(2), 938–950.
- Martin, R. E., Kemppainen, P., Masuda, Y., Yao, D., Murray, G. M., & Sessle, B. J. (1999). Features of cortically evoked swallowing in the awake primate (*Macaca fascicularis*). *Journal of Neurophysiology*, 82(3), 1529–1541.
- Martin, R. E., MacIntosh, B. J., Smith, R. C., Barr, A. M., Stevens, T. K., Gati, J. S., & Menon, R. S. (2004). Cerebral areas processing swallowing and tongue movement are overlapping but distinct: a functional magnetic resonance imaging study. *Journal of Neurophysiology*, 92(4), 2428–2443.
- Martin, R. E., Murray, G. M., Kemppainen, P., Masuda, Y., & Sessle, B. J. (1997). Functional properties of neurons in the primate tongue primary motor cortex during swallowing. *Journal of Neurophysiology*, 78(3), 1516–1530. Am Physiological Soc.
- Martin, R. E., & Sessle, B. J. (1993). The role of the cerebral cortex in swallowing. *Dysphagia*, 8(3), 195–202.

- Martin-Harris, B., Brodsky, M. B., Michel, Y., Lee, F.-S., & Walters, B. (2007). Delayed initiation of the pharyngeal swallow: normal variability in adult swallows. *Journal of Speech, Language, and Hearing Research*, 50(3), 585–594.
- Martin-Harris, B., Michel, Y., & Castell, D. O. (2005). Physiologic model of oropharyngeal swallowing revisited. *Otolaryngology-Head and Neck Surgery*, 133(2), 234–40.
- Martino, R., Foley, N., Bhogal, S., Diamant, N., Speechley, M., & Teasell, R. W. (2005). Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. *Stroke; a journal of cerebral circulation*, 36(12), 2756–63.
- Martino, R., Terrault, N., Ezerzer, F., Mikulis, D., & Diamant, N. E. (2001). Dysphagia in a Patient With Lateral Medullary Syndrome: Insight Into the Central Control of Swallowing. *Gastroenterology*, 121(2), 420–426.
- Mathiassen, S. E., Winkel, J., & Hägg, G. M. (1995). Normalization of surface EMG amplitude from the upper trapezius muscle in ergonomic studies - A review. *Journal of Electromyography and Kinesiology*, 5(4), 197–226.
- Matsunaga, K., Uozumi, T., Tsuji, S., & Murai, Y. (1998). Age-dependent changes in physiological threshold asymmetries for the motor evoked potential and silent period following transcranial magnetic stimulation. *Electroencephalography and Clinical Neurophysiology*, 109(6), 502–507.
- Matsuo, K., & Palmer, J. B. (2009). Coordination of Mastication, Swallowing and Breathing. *The Japanese Dental Science Review*, 45(1), 31–40.
- Mattay, V. S., Fera, F., Tessitore, A., Hariri, A. R., Das, S., Callicott, J. H., & Weinberger, D. R. (2002). Neurophysiological correlates of age-related changes in human motor function. *Neurology*, 58(4), 630–635.
- McAdam, D. W., & Whitaker, H. A. (1971). Language production: electroencephalographic localization in the normal human brain. *Science*, 172(3982), 499–502.
- McCall, G. E., Byrnes, W. C., Dickinson, A., Pattany, P. M., & Fleck, S. J. (1996a). Muscle fiber hypertrophy, hyperplasia, and capillary density in college men after resistance training. *Journal of Applied Physiology*, 81(5), 2004–2012.
- McConnel, F. M. (1988). Analysis of pressure generation and bolus transit during pharyngeal swallowing. *The Laryngoscope*, 98(1), 71–78.
- McConnel, F. M., Cerenko, D., Jackson, R. T., & Guffin, T. N. (1988). Timing of major events of pharyngeal swallowing. *Archives of Otolaryngology-Head & Neck Surgery*, 114(12), 1413–1418.
- McGill, K. C. (2004). Surface electromyogram signal modelling. *Medical & Biological Engineering & Computing*, 42(4), 446–454.
- McHorney, C. A., Bricker, D. E., Kramer, A. E., Rosenbek, J. C., Robbins, J. A., Chignell, K. A., Logemann, J. A., et al. (2000). The SWAL-QOL outcomes tool for oropharyngeal dysphagia in adults: I. Conceptual foundation and item development. *Dysphagia*, 15(3), 115–121.

- McHorney, C. A., Bricker, D. E., Robbins, J. A., Kramer, A. E., Rosenbek, J. C., & Chignell, K. A. (2000). The SWAL-QOL outcomes tool for oropharyngeal dysphagia in adults: II. Item reduction and preliminary scaling. *Dysphagia*, 15(3), 122–133.
- McLester, J. R., Bishop, P. A., Smith, J., Wyers, L., Dale, B., Kozusko, J., Richardson, M., et al. (2003). A series of studies-a practical protocol for testing muscular endurance recovery. *Journal of Strength and Conditioning Research*, 17(2), 259–273.
- McManus, L. J., Dawes, P. J. D., & Stringer, M. D. (2011). Clinical anatomy of the chorda tympani: a systematic review. *The Journal of Laryngology and Otology*, 125(11), 1101–1108.
- McNevin, N. H., Wulf, G., & Carlson, C. (2000). Effects of attentional focus, self-control, and dyad training on motor learning: implications for physical rehabilitation. *Physical Therapy*, 80(4), 373–385.
- van der Meché, F. G., & van Gijn, J. (1986). Hypotonia: an erroneous clinical concept? *Brain*, 109(6), 1169–1178.
- Meng, N. H., Wang, T. G., & Lien, I. N. (2000). Dysphagia in patients with brainstem stroke: incidence and outcome. *American Journal of Physical Medicine & Rehabilitation*, 79(2), 170–175.
- Merson, R. M., & Rolnick, M. I. (1998). Speech-language pathology and dysphagia in multiple sclerosis. *Physical Medicine and Rehabilitation Clinics of North America*, 9(3), 631–641.
- Merton, P. A., Hill, D. K., Morton, H. B., & Marsden, C. D. (1982). Scope of a technique for electrical stimulation of human brain, spinal cord, and muscle. *Lancet*, 2(8298), 597–600.
- Miller, A. J. (1982). Deglutition. *Physiological Reviews*, 62(1), 129–184.
- Miller, A. J. (2008). The neurobiology of swallowing and dysphagia. *Developmental Disabilities Research Reviews*, 14(2), 77–86.
- Miller, F. R. (1920). The cortical paths for mastication and deglutition. *The Journal of Physiology*, 53(6), 473–478.
- Miller, N., Allcock, L., Hildreth, a J., Jones, D., Noble, E., & Burn, D. J. (2009). Swallowing problems in Parkinson disease: frequency and clinical correlates. *Journal of Neurology, Neurosurgery, and Psychiatry*, 80(9), 1047–1049.
- Miller, N., Deane, K. H. O., Jones, D., Noble, E., & Gibb, C. (2010). National survey of speech and language therapy provision for people with Parkinson's disease in the United Kingdom: therapists' practices. *International Journal of Language & Communication Disorders*, 46(2), 189–201.
- Miller, N., Noble, E., Jones, D., & Burn, D. (2006). Hard to swallow: dysphagia in Parkinson's disease. *Age and Ageing*, 35(6), 614–618.
- Mills, K. R. (1999). Magnetic brain stimulation: a review after 10 years experience. *Electroencephalography and Clinical Neurophysiology*, 49, 239–244.

- Milner-Brown, H. S., & Stein, R. B. (1975). The relation between the surface electromyogram and muscular force. *The Journal of Physiology*, 246(3), 549–569.
- Milner-Brown, H. S., Stein, R. B., & Lee, R. G. (1975). Synchronization of human motor units: possible roles of exercise and supraspinal reflexes. *Electroencephalography and Clinical Neurophysiology*, 38(3), 245–254.
- Ministry of Health. (2008). *A Portrait of Health: Key results of the 2006/07 New Zealand Health Survey*. Health (San Francisco). Wellington: Ministry of Health.
- Mittal, K. R., & Logmani, F. H. (1987). Age-related reduction in 8th cervical ventral nerve root myelinated fiber diameters and numbers in man. *Journal of Gerontology*, 42(1), 8–10.
- Moffroid, M. T., & Kusiak, E. T. (1975). The power struggle: definition and evaluation of power of muscular performance. *Physical Therapy*, 55(10), 1098–1104.
- Molfenter, S. M., & Steele, C. M. (2011). Physiological variability in the deglutition literature: hyoid and laryngeal kinematics. *Dysphagia*, 26(1), 67–74.
- Monfils, M.-H., Plautz, E. J., & Kleim, J. A. (2005). In search of the motor engram: motor map plasticity as a mechanism for encoding motor experience. *The Neuroscientist*, 11(5), 471–483.
- Moritani, T. (1993). Neuromuscular adaptations during the acquisition of muscle strength, power and motor tasks. *Journal of Biomechanics*, 26(1), 95–107. Elsevier.
- Moritani, T., & DeVries, H. A. (1979). Neural factors versus hypertrophy in the time course of muscle strength gain. *American Journal of Physical Medicine & Rehabilitation*, 58(3), 115–130.
- Morris, M. E., Martin, C. L., & Schenkman, M. L. (2010). Striding out with Parkinson disease: evidence-based physical therapy for gait disorders. *Physical Therapy*, 90(2), 280–288.
- Morris, S. L., Dodd, K. J., & Morris, M. E. (2004). Outcomes of progressive resistance strength training following stroke: a systematic review. *Clinical Rehabilitation*, 18(1), 27–39.
- Mosier, K. M., & Bereznaya, I. (2001). Parallel cortical networks for volitional control of swallowing in humans. *Experimental Brain Research*, 140(3), 280–289.
- Mosier, K. M., Liu, W. C., Maldjian, J., Shah, R., & Modi, B. (1999). Lateralization of cortical function in swallowing: a functional MR imaging study. *American Journal of Neuroradiology*, 20(8), 1520–1526.
- Mosier, K. M., Patel, R., Liu, W. C., Kalnin, A., Maldjian, J., & Baredes, S. (1999). Cortical representation of swallowing in normal adults: functional implications. *The Laryngoscope*, 109(9), 1417–1423.
- Mountcastle, V. B. (1997). The columnar organization of the neocortex. *Brain*, 120(4), 701–722.
- Mu, L., & Sanders, I. (2010). Human tongue neuroanatomy: Nerve supply and motor endplates. *Clinical Anatomy*, 791, 777–791.

- Muellbacher, W., Artner, C., & Mamoli, B. (1999). The role of the intact hemisphere in recovery of midline muscles after recent monohemispheric stroke. *Journal of Neurology*, 246(4), 250–256.
- Muellbacher, W., Ziemann, U., Boroojerdi, B., Cohen, L. G., & Hallett, M. (2001). Role of the human motor cortex in rapid motor learning. *Experimental Brain Research*, 136(4), 431–438. Springer.
- Mutch, W. J., Strudwick, A., Roy, S. K., & Downie, A. W. (1986). Parkinson's disease: disability, review, and management. *British Medical Journal*, 293(6548), 675–677.
- Nagaya, M., Kachi, T., & Yamada, T. (2000). Effect of swallowing training on swallowing disorders in Parkinson's disease. *Scandinavian Journal of Rehabilitation Medicine*, 32(1), 11–15. Informa Healthcare.
- Nagaya, M., Kachi, T., Yamada, T., & Igata, A. (1998). Videofluorographic study of swallowing in Parkinson's disease. *Dysphagia*, 13(2), 95–100.
- Nagaya, M., Kachi, T., Yamada, T., & Sumi, Y. (2004). Videofluorographic observations on swallowing in patients with dysphagia due to neurodegenerative diseases. *Nagoya Journal of Medical Science*, 67(1-2), 17–23.
- Nakagawa, S. (2004). A farewell to Bonferroni: the problems of low statistical power and publication bias. *Behavioral Ecology*, 15(6), 1044–1045.
- Nakane, A., Tohara, H., Ouchi, Y., Goto, S., & Uematsu, H. (2006). Videofluoroscopic kinesiological analysis of swallowing: defining a standard plane. *Journal of Medical and Dental Sciences*, 53(1), 7–15.
- Neilson, P. D., Andrews, G., Guitar, B. E., & Quinn, P. T. (1979). Tonic stretch reflexes in lip, tongue and jaw muscles. *Brain Research*, 178(2-3), 311–327.
- Nicosia, M. A., Hind, J. A., Roecker, E. B., Carnes, M., Doyle, J., Dengel, G. A., & Robbins, J. A. (2000). Age effects on the temporal evolution of isometric and swallowing pressure. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 55(11), M634–640.
- Niederman, M. S. (1998). Community-acquired pneumonia: a North American perspective. *Chest*, 113(3 Suppl), 179S–182S.
- Niyazov, D. M., Butler, A. J., Kadah, Y. M., Epstein, C. M., & Hu, X. P. (2005). Functional magnetic resonance imaging and transcranial magnetic stimulation: effects of motor imagery, movement and coil orientation. *Clinical Neurophysiology*, 116(7), 1601–1610.
- Nollet, H. (2003). Transcranial magnetic stimulation: review of the technique, basic principles and applications. *The Veterinary Journal*, 166(1), 28–42.
- Nolte, J. (2002). *The human brain: an introduction to its functional anatomy* (5th ed.). St. Louis: Mosby-Elsevier.
- Norcross, M. F., Blackburn, J. T., & Goerger, B. M. (2010). Reliability and interpretation of single leg stance and maximum voluntary isometric contraction methods of

- electromyography normalization. *Journal of Electromyography and Kinesiology*, 20(3), 420–5.
- Nordstrom, M. A. (2007). Insights into the bilateral cortical control of human masticatory muscles revealed by transcranial magnetic stimulation. *Archives of Oral Biology*, 52(4), 338–342.
- Nordstrom, M. A., Miles, T. S., Gooden, B. R., Butler, S. L., Ridding, M. C., & Thompson, P. D. (1999). Motor cortical control of human masticatory muscles. *Progress in Brain Research*, 123, 203–214.
- Nudo, R. J. (2003). Adaptive plasticity in motor cortex: implications for rehabilitation after brain injury. *Journal of Rehabilitation Medicine*, 41, 7–10. Stockholm, Sweden: Taylor & Francis, c2003-.
- Nudo, R. J. (2006a). Plasticity. *NeuroRx*, 3(4), 420–427.
- Nudo, R. J. (2006b). Mechanisms for recovery of motor function following cortical damage. *Current Opinion in Neurobiology*, 16(6), 638–644.
- Nudo, R. J. (2007). Postinfarct cortical plasticity and behavioral recovery. *Stroke*, 38(2), 840–845.
- Nudo, R. J., & Milliken, G. W. (1996). Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys. *Journal of Neurophysiology*, 75(5), 2144–2149.
- Nussenblatt, R. B., Marincola, F. M., & Schechter, A. N. (2010). Translational medicine-doing it backwards. *Journal of Translational Medicine*, 8(12), 1–3.
- Odderson, I. R., Keaton, J. C., & McKenna, B. S. (1995). Swallow management in patients on an acute stroke pathway: quality is cost effective. *Archives of Physical Medicine and Rehabilitation*, 76(12), 1130–1133.
- Oelschlager, B. K., Chang, L., Pope, C. E., & Pellegrini, C. a. (2005). Typical GERD symptoms and esophageal pH monitoring are not enough to diagnose pharyngeal reflux. *The Journal of Surgical Research*, 128(1), 55–60.
- Ohmae, Y., Logemann, J. A., Kaiser, P., Hanson, D. G., & Kahrilas, P. J. (1995). Timing of glottic closure during normal swallow. *Head & Neck*, 17(5), 394–402.
- Oliviero, A., Profice, P., Tonali, P. a, Pilato, F., Saturno, E., Dileone, M., Ranieri, F., et al. (2006). Effects of aging on motor cortex excitability. *Neuroscience Research*, 55(1), 74–77.
- Ollivier, K., Portero, P., Maïsetti, O., & Hogrel, J.-Y. (2005). Repeatability of surface EMG parameters at various isometric contraction levels and during fatigue using bipolar and Laplacian electrode configurations. *Journal of Electromyography and Kinesiology*, 15(5), 466–473.
- Olsson, R., Castell, J. A., Castell, D. O., & Ekberg, O. (1995). Solid-state computerized manometry improves diagnostic yield in pharyngeal dysphagia: simultaneous videoradiography and manometry in dysphagia patients with normal barium swallows. *Abdominal imaging*, 20(3), 230–235.

- Olsson, R., Nilsson, H., & Ekberg, O. (1995). Simultaneous videoradiography and pharyngeal solid state manometry (videomanometry) in 25 nondysphagic volunteers. *Dysphagia*, 10(1), 36–41.
- Ortu, E., Deriu, F., Suppa, A., Giaconi, E., Tolu, E., & Rothwell, J. C. (2008). Intracortical modulation of cortical-bulbar responses for the masseter muscle. *The Journal of Physiology*, 586(14), 3385–3404.
- Ottenhoff, F. A., van der Bilt, A., van der Glas, H. W., Bosman, F., & Abbink, J. H. (1996). The relationship between jaw elevator muscle surface electromyogram and simulated food resistance during dynamic condition in humans. *Journal of Oral Rehabilitation*, 23(4), 270–279.
- Palmer, J. B. (1998). Bolus aggregation in the oropharynx does not depend on gravity. *Archives of Physical Medicine and Rehabilitation*, 79(6), 691–696. Elsevier.
- Palmer, J. B., Drennan, J. C., & Baba, M. (2000). Evaluation and treatment of swallowing impairments. *American Family Physician*, 61(8), 2453–2462. WB SAUNDERS CO.
- Palmer, J. B., Hiiemae, K. M., & Liuf, J. (1997). Tongue-jaw linkages in human feeding: a preliminary videofluorographic study. *Archives of Oral Biology*, 42(6), 429–441. Elsevier.
- Palmer, J. B., Rudin, N. J., Lara, G., & Crompton, A. W. (1992). Coordination of mastication and swallowing. *Dysphagia*, 7(4), 187–200. Springer.
- Palmer, J. B., Tanaka, E., & Ensrud, E. (2000). Motions of the posterior pharyngeal wall in human swallowing: a quantitative videofluorographic study. *Archives of Physical Medicine and Rehabilitation*, 81(11), 1520–1526.
- Palmer, J. B., Tanaka, E., & Siebens, A. A. (1988). Motions of the posterior pharyngeal wall in swallowing. *The Laryngoscope*, 98(4), 414–417. Wiley Online Library.
- Palmer, P. M., Luschei, E., Jaffe, D., & McCulloch, T. M. (1999). Contributions of individual muscles to the submental surface electromyogram during swallowing. *Journal of Speech, Language, and Hearing Research*, 42(6), 1378–1391.
- Parker, C., Power, M. L., Hamdy, S., Bowen, A., Tyrrell, P., & Thompson, D. G. (2004). Awareness of dysphagia by patients following stroke predicts swallowing performance. *Dysphagia*, 19(1), 28–35.
- Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. B. (2005). The plastic human brain cortex. *Annual Review of Neuroscience*, 28, 377–401.
- Pascual-Leone, A., Freitas, C., Oberman, L., Horvath, J. C., Halko, M., Eldaief, M., Bashir, S., et al. (2011). Characterizing brain cortical plasticity and network dynamics across the age-span in health and disease with TMS-EEG and TMS-fMRI. *Brain Topography*, 24(3-4), 302–315.
- Pascual-Leone, A., Nguyet, D., Cohen, L. G., Brasil-Neto, J. P., Cammarota, A., & Hallett, M. (1995). Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor skills. *Journal of Neurophysiology*, 74(3), 1037–1045.

- Pascual-Leone, A., Tarazona, F., & Catalá, M. D. (1999). Applications of transcranial magnetic stimulation in studies on motor learning. *Electroencephalography and Clinical Neurophysiology*, 51, 157–161.
- Patten, C., Kamen, G., & Rowland, D. M. (2001). Adaptations in maximal motor unit discharge rate to strength training in young and older adults. *Muscle & Nerve*, 24(4), 542–550.
- Patton, H. D., & Amassian, V. E. (1954). Single and multiple-unit analysis of cortical stage of pyramidal tract activation. *Journal of Neurophysiology*, 17(4), 345–363.
- Pauloski, B. R. (2008). Rehabilitation of dysphagia following head and neck cancer. *Physical Medicine and Rehabilitation Clinics of North America*, 19(4), 889–928, x.
- Pauloski, B. R., Rademaker, A. W., Lazarus, C. L., Boeckxstaens, G., Kahrilas, P. J., & Logemann, J. A. (2009). Relationship between manometric and videofluoroscopic measures of swallow function in healthy adults and patients treated for head and neck cancer with various modalities. *Dysphagia*, 24(2), 196–203.
- De Pauw, A., Dejaeger, E., D'hooghe, B., & Carton, H. (2002). Dysphagia in multiple sclerosis. *Clinical Neurology and Neurosurgery*, 104(4), 345–351.
- Pearce, A. J., Thickbroom, G. W., Byrnes, M. L., & Mastaglia, F. L. (2000). Functional reorganisation of the corticomotor projection to the hand in skilled racquet players. *Experimental Brain Research*, 130(2), 238–243.
- Pearce, S. L., Miles, T. S., Thompson, P. D., & Nordstrom, M. a. (2003). Is the long-latency stretch reflex in human masseter transcortical? *Experimental Brain Research*, 150(4), 465–472.
- Pearson, W. G., Langmore, S. E., Yu, L. B., & Zumwalt, A. C. (2012). Structural Analysis of Muscles Elevating the Hyolaryngeal Complex. *Dysphagia*.
- Pedersen, A. M., Bardow, A., Jensen, S. B., & Nauntofte, B. (2002). Saliva and gastrointestinal functions of taste, mastication, swallowing and digestion. *Oral Diseases*, 8(3), 117–129.
- Peinemann, A., Lehner, C., Conrad, B., & Siebner, H. R. (2001). Age-related decrease in paired-pulse intracortical inhibition in the human primary motor cortex. *Neuroscience Letters*, 313(1-2), 33–36.
- Peinemann, A., Reimer, B., Löer, C., Quartarone, A., Münchau, A., Conrad, B., & Siebner, H. R. (2004). Long-lasting increase in corticospinal excitability after 1800 pulses of subthreshold 5 Hz repetitive TMS to the primary motor cortex. *Clinical Neurophysiology*, 115(7), 1519–1526.
- Peng, C. L., Jost-Brinkmann, P. G., & Miethke, R. R. (1996). The cushion scanning technique: a method of dynamic tongue sonography and its comparison with the transducer-skin coupling scanning technique during swallowing. *Academic Radiology*, 3(3), 239–244.
- Van Peppen, R., Kwakkel, G., Wood-Dauphinee, S., Hendriks, H., Van der Wees, P., & Dekker, J. (2004). The impact of physical therapy on functional outcomes after stroke: what's the evidence? *Clinical Rehabilitation*, 18(8), 833–862.

- Perlman, A. L., Palmer, P. M., McCulloch, T. M., & Vandaele, D. J. (1999a). Electromyographic activity from human laryngeal, pharyngeal, and submental muscles during swallowing. *Journal of applied physiology*, 86(5), 1663–9.
- Perlman, A. L., Palmer, P. M., McCulloch, T. M., & Vandaele, D. J. (1999b). Electromyographic activity from human laryngeal, pharyngeal, and submental muscles during swallowing. *Journal of Applied Physiology*, 86(5), 1663–9.
- Perlman, A. L., & Schulze-Delrieu, K. (1996). *Deglutition and its disorders: anatomy, physiology, clinical diagnosis, and management*. San Diego, CA: Singular publisher group.
- Phillips, C. V. (2004). Publication bias in situ. *Medical Research Methodology*, 4(20), 1–11.
- Piron, L., Piccione, F., Tonin, P., & Dam, M. (2005). Clinical correlation between motor evoked potentials and gait recovery in poststroke patients. *Archives of Physical Medicine and Rehabilitation*, 86(9), 1874–1878.
- Pitcher, J. B., Ogston, K. M., & Miles, T. S. (2002). Age and sex differences in human motor cortex input-output characteristics. *The Journal of Physiology*, 546(2), 605–613.
- Pitts, T., Bolser, D., Rosenbek, J. C., Troche, M., Okun, M. S., & Sapienza, C. (2009). Impact of expiratory muscle strength training on voluntary cough and swallow function in Parkinson disease. *Chest*, 135(5), 1301–1308.
- Platz, T., Brown, R. G., & Marsden, C. D. (1998). Training improves the speed of aimed movements in Parkinson's disease. *Brain*, 121(3), 505–514.
- Plautz, E. J., Milliken, G. W., & Nudo, R. J. (2000). Effects of repetitive motor training on movement representations in adult squirrel monkeys: role of use versus learning. *Neurobiology of Learning and Memory*, 74(1), 27–55.
- Plowman, E. K., Triggs, W. J., Malcolm, M. P., & Rosenbek, J. C. (2008). Reliability of transcranial magnetic stimulation for mapping swallowing musculature in the human motor cortex. *Clinical Neurophysiology*, 119(10), 2298–2303.
- Power, M. L., Fraser, C. H., Hobson, A., Rothwell, J. C., Mistry, S., Nicholson, D. A., Thompson, D. G., et al. (2004). Changes in pharyngeal corticobulbar excitability and swallowing behavior after oral stimulation. *American Journal of Physiology. Gastrointestinal and Liver Physiology*, 286(1), G45–50.
- Power, M. L., Hamdy, S., Singh, S., Tyrrell, P. J., Turnbull, I., & Thompson, D. G. (2007). Deglutitive laryngeal closure in stroke patients. *Journal of Neurology, Neurosurgery, and Psychiatry*, 78(2), 141–146.
- Powers, S., & Howley, E. (2001). *Exercise Physiology: Theory and application to fitness and performance* (6th ed.). Boston: McGraw-Hill.
- Prades, J.-M., Timoshenko, A. P., Asanau, A., Gavid, M., Benakki, H., Dubois, M.-D., Faye, M. B., et al. (2009). The cricopharyngeal muscle and the laryngeal nerves: contribution to the functional anatomy of swallowing. *Morphologie*, 93(301), 35–41.
- Prasad, S., & Galetta, S. (2007). The Trigeminal Nerve. In C. G. Goetz (Ed.), *Textbook of Clinical Neurology* (3rd ed., pp. 165–183). Philadelphia, PA: Elsevier Inc.

- Priefer, B. A., & Robbins, J. A. (1997). Eating changes in mild-stage Alzheimer's disease: a pilot study. *Dysphagia*, 12(4), 212–221.
- Proteau, L., Marteniuk, R. G., & Lévesque, L. (1992). A sensorimotor basis for motor learning: evidence indicating specificity of practice. *The Quarterly Journal of Experimental Psychology*, 44(3), 557–575.
- Quartarone, A., Bagnato, S., Rizzo, V., Morgante, F., Sant'angelo, A., Battaglia, F., Messina, C., et al. (2005). Distinct changes in cortical and spinal excitability following high-frequency repetitive TMS to the human motor cortex. *Experimental Brain Research*, 161(1), 114–124.
- Ramig, L. O., Sapis, S., Countryman, S., Pawlas, A. A., O'Brien, C., Hoehn, M., & Thompson, L. L. (2001). Intensive voice treatment (LSVT) for patients with Parkinson's disease: a 2 year follow up. *Journal of Neurology, Neurosurgery, and Psychiatry*, 71(4), 493–498. BMJ Publishing Group Ltd.
- Ranganathan, R., & Newell, K. M. (2010). Motor learning through induced variability at the task goal and execution redundancy levels. *Journal of Motor Behavior*, 42(5), 307–316.
- Raue, U., Trappe, T. A., Estrem, S. T., Qian, H.-R., Helvering, L. M., Smith, R. C., & Trappe, S. (2012). Transcriptome signature of resistance exercise adaptations: mixed muscle and fiber type specific profiles in young and old adults. *Journal of Applied Physiology*, 112(10), 1625–1636.
- Reddy, N. P., Simcox, D. L., Gupta, V., Motta, G. E., Coppenger, J., Das, A., & Buch, O. (2000). Biofeedback therapy using accelerometry for treating dysphagic patients with poor laryngeal elevation: case studies. *Journal of Rehabilitation Research and Development*, 37(3), 361–372.
- Remple, M. S., Bruneau, R. M., VandenBerg, P. M., Goertzen, C., & Kleim, J. A. (2001). Sensitivity of cortical movement representations to motor experience: evidence that skill learning but not strength training induces cortical reorganization. *Behavioural Brain Research*, 123(2), 133–141. Elsevier.
- Remy, J., Wegrowski, J., Crechet, F., Martin, M., & Daburon, F. (1991). Long-term overproduction of collagen in radiation-induced fibrosis. *Radiation Research*, 125(1), 14–19.
- Ren, J., Shaker, R., Zamir, Z., Dodds, W. J., Hogan, W. J., & Hoffmann, R. G. (1993). Effect of age and bolus variables on the coordination of the glottis and upper esophageal sphincter during swallowing. *The American Journal of Gastroenterology*, 88(5), 665–669.
- Reuter-Lorenz, P. A., Jonides, J., Smith, E. E., Hartley, A., Miller, A. J., Marshuetz, C., & Koeppe, R. A. (2000). Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. *Journal of Cognitive Neuroscience*, 12(1), 174–187.
- Riecker, A., Gröschel, K., Ackermann, H., Steinbrink, C., Witte, O., & Kastrup, A. (2006). Functional significance of age-related differences in motor activation patterns. *NeuroImage*, 32(3), 1345–1354.
- Rioult-Pedotti, M. S., Friedman, D., & Donoghue, J. P. (2000). Learning-induced LTP in neocortex. *Science*, 290(5491), 533–536.

- Robbins, J. A., Butler, S. G., Daniels, S. K., Diez Gross, R., Langmore, S. E., Lazarus, C. L., Martin-Harris, B., et al. (2008). Swallowing and dysphagia rehabilitation: translating principles of neural plasticity into clinically oriented evidence. *Journal of Speech, Language, and Hearing Research*, 51(1), S276–300.
- Robbins, J. A., Gangnon, R. E., Theis, S. M., Kays, S. A., Hewitt, A. L., & Hind, J. A. (2005). The effects of lingual exercise on swallowing in older adults. *Journal of the American Geriatrics Society*, 53(9), 1483–1489.
- Robbins, J. A., Hamilton, J. W., Lof, G. L., & Kempster, G. B. (1992). Oropharyngeal swallowing in normal adults of different ages. *Gastroenterology*, 103(3), 823–829.
- Robbins, J. A., Kays, S. A., Gangnon, R. E., Hind, J. A., Hewitt, A. L., Gentry, L. R., & Taylor, A. J. (2007). The effects of lingual exercise in stroke patients with dysphagia. *Archives of Physical Medicine and Rehabilitation*, 88(2), 150–158.
- Robbins, J. A., & Levin, R. L. (1988). Swallowing after unilateral stroke of the cerebral cortex: preliminary experience. *Dysphagia*, 3(1), 11–17.
- Robbins, J. A., Levine, R. L., Maser, A., Rosenbek, J. C., & Kempster, G. B. (1993). Swallowing after unilateral stroke of the cerebral cortex. *Archives of Physical Medicine and Rehabilitation*, 74(12), 1295–1300.
- Robbins, J. A., Levine, R., Wood, J., Roecker, E. B., & Luschei, E. (1995). Age effects on lingual pressure generation as a risk factor for dysphagia. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 50(5), M257–262.
- Robbins, J. A., Logemann, J. A., & Kirshner, H. S. (1986). Swallowing and speech production in Parkinson's disease. *Annals of Neurology*, 19(3), 283–287.
- Robey, R. R. (2004a). A five-phase model for clinical-outcome research. *Journal of Communication Disorders*, 37(5), 401–411.
- Robey, R. R. (2004b). Reporting point and interval estimates of effect-size for planned contrasts: fixed within effect analyses of variance. *Journal of Fluency Disorders*, 29(4), 307–341.
- Robey, R. R., & Schultz, M. C. (1998). A model for conducting clinical-outcome research: An adaptation of the standard protocol for use in aphasiology. *Aphasiology*, 12(9), 787–810.
- Rodrigues, B., Nóbrega, A. C., Sampaio, M., Argolo, N., & Melo, A. (2011). Silent saliva aspiration in Parkinson's disease. *Movement Disorders*, 26(1), 138–141.
- Rodriguez, A. A., & Agre, J. C. (1991). Correlation of motor units with strength and spectral characteristics in polio survivors and controls. *Muscle & Nerve*, 14(5), 429–434.
- Rogasch, N. C., Dartnall, T. J., Cirillo, J., Nordstrom, M. A., & Semmler, J. G. (2009). Corticomotor plasticity and learning of a ballistic thumb training task are diminished in older adults. *Journal of Applied Physiology*, 107(6), 1874–1883.
- Rose, D. J., & Robert, W. C. (2006). *Multilevel Approach to the Study of Motor Control and Learning* (2nd ed.). San Francisco: Pearson/Benjamin Cummings.
- Rosenbek, J. C. (1995). Efficacy in dysphagia. *Dysphagia*, 10, 263–267.

- Rosenbek, J. C., Robbins, J. A., Willford, W. O., Kirk, G., Schiltz, a, Sowell, T. W., Deutsch, S. E., et al. (1998). Comparing treatment intensities of tactile-thermal application. *Dysphagia*, 13(1), 1–9.
- Rosenkranz, K., Kacar, A., & Rothwell, J. C. (2007). Differential modulation of motor cortical plasticity and excitability in early and late phases of human motor learning. *The Journal of Neuroscience*, 27(44), 12058–12066.
- Rosenthal, J., Waller, H. J., & Amassian, V. E. (1967). An analysis of the activation of motor cortical neurons by surface stimulation. *Journal of Neurophysiology*, 30(4), 844–858.
- Rossini, P. M., Caltagirone, C., Castriota-Scanderbeg, A., Cicinelli, P., Del Gratta, C., Demartin, M., Pizzella, V., et al. (1998). Hand motor cortical area reorganization in stroke: a study with fMRI, MEG and TCS maps. *Neuroreport*, 9(9), 2141–6.
- Rossini, P. M., Desiato, M. T., & Caramia, M. D. (1992). Age-related changes of motor evoked potentials in healthy humans: non-invasive evaluation of central and peripheral motor tracts excitability and conductivity. *Brain Research*, 593(1), 14–19.
- Rostami, H. R., & Ashayeri, H. (2009). Effects of motor skill practice on reaction time and learning retention in Parkinson's disease. *Neurology India*, 57(6), 768–771.
- Roth, S. M., Ivey, F. M., Martel, G. F., Lemmer, J. T., Hurlbut, D. E., Siegel, E. L., Metter, E. J., et al. (2001). Muscle size responses to strength training in young and older men and women. *Journal of the American Geriatrics Society*, 49(11), 1428–1433.
- Rothwell, J. C. (1997). Techniques and mechanisms of action of transcranial stimulation of the human motor cortex. *Journal of Neuroscience Methods*, 74(2), 113–122.
- Rugiu, M. G. (2007). Role of videofluoroscopy in evaluation of neurologic dysphagia. *Acta Otorhinolaryngologica Italica*, 27(6), 306–316.
- Ruschena, D., Mullen, P. E., Palmer, S., Burgess, P., Cordner, S. M., Drummer, O. H., Wallace, C., et al. (2003). Choking deaths: the role of antipsychotic medication. *The British Journal of Psychiatry*, 183, 446–450.
- Rushall, B., & Pyke, F. (1990). *Training for sports and fitness*. Melbourne: Macmillan Education.
- Russell, J. A., Ciucci, M. R., Connor, N. P., & Schallert, T. (2010). Targeted exercise therapy for voice and swallow in persons with Parkinson's disease. *Brain Research*, 1341, 3–11. Elsevier B.V.
- Rutherford, O. M., & Jones, D. A. (1986). The role of learning and coordination in strength training. *European Journal of Applied Physiology and Occupational Physiology*, 55(1), 100–105.
- Rösler, K. M., Petrow, E., Mathis, J., Arányi, Z., Hess, C. W., & Magistris, M. R. (2002). Effect of discharge desynchronization on the size of motor evoked potentials: an analysis. *Clinical Neurophysiology*, 113(11), 1680–1687.
- Rösler, K. M., Roth, D. M., & Magistris, M. R. (2008). Trial-to-trial size variability of motor-evoked potentials. A study using the triple stimulation technique. *Experimental Brain Research*, 187(1), 51–59.

- Sale, D. G., MacDougall, J. D., Upton, A. R., & McComas, A. J. (1983). Effect of strength training upon motoneuron excitability in man. *Medicine and Science in Sports and Exercise*, 15(1), 57–62.
- Salmoni, A. W., Schmidt, R. A., & Walter, C. B. (1984). Knowledge of results and motor learning: a review and critical reappraisal. *Psychological Bulletin*, 95(3), 355–386.
- Salvador, R., Silva, S., Basser, P. J., & Miranda, P. C. (2011). Determining which mechanisms lead to activation in the motor cortex: a modeling study of transcranial magnetic stimulation using realistic stimulus waveforms and sulcal geometry. *Clinical Neurophysiology*, 122(4), 748–758. International Federation of Clinical Neurophysiology.
- Sarfeld, A.-S., Diekhoff, S., Wang, L. E., Liuzzi, G., Uludağ, K., Eickhoff, S. B., Fink, G. R., et al. (2012). Convergence of human brain mapping tools: neuronavigated TMS parameters and fMRI activity in the hand motor area. *Human Brain Mapping*, 33(5), 1107–23.
- Sasaki, C. T., Kim, Y. H., Sims, H. S., & Czibulka, A. (1999). Motor innervation of the human cricopharyngeus muscle. *The Annals of Otology, Rhinology, and Laryngology*, 108(12), 1132–1139.
- Savage, J. (1998). *Fundamental strength training*. Minneapolis, MN: Learner Publications.
- Scarborough, D. R., Waizenhofer, S., Siekemeyer, L., & Hughes, M. (2010). Sonographically measured hyoid bone displacement during swallow in preschool children: a preliminary study. *Journal of Clinical Ultrasound*, 38(8), 430–434.
- Schell, G. R., & Strick, P. L. (1984). The origin of thalamic inputs to the arcuate premotor and supplementary motor areas. *The Journal of Neuroscience*, 4(2), 539–560.
- Schindler, A., Ginocchio, D., & Ruoppolo, G. (2008). What we don't know about dysphagia complications? *Revue de Laryngologie Otologie Rhinologie*, 129(2), 75–78.
- Schmidt, R. A., & Lee, T. D. (1999). *Motor control and learning: A behavioral emphasis* (3rd ed.). Champaign, IL: Human Kinetics.
- Schmidt, R. A., & Wrisberg, C. A. (2008). *Motor learning and performance: a situation based learning approach* (4th Ed.). Champaign, IL: Human Kinetics Publishers.
- Scholten, R. R., Pillen, S., Verrips, a, & Zwarts, M. J. (2003). Quantitative ultrasonography of skeletal muscles in children: normal values. *Muscle & nerve*, 27(6), 693–8.
- Sciote, J. J., Horton, M. J., Rowleson, A. M., & Link, J. (2003). Specialized cranial muscles: how different are they from limb and abdominal muscles? *Cells, Tissues, Organs*, 174(1-2), 73–86.
- Segura, M. J., Bueri, J. A., Gandolfo, C. N., Simonetti, D. D., Herrera, G. A., & Sica, R. E. (1995). Motor activation time in Parkinson's disease. *Medicina*, 55(3), 208–12.
- Semmler, J. G., & Nordstrom, M. A. (1998). Motor unit discharge and force tremor in skill- and strength-trained individuals. *Experimental Brain Research*, 119(1), 27–38.

- Semmler, J. G., Sale, M. V, Meyer, F. G., & Nordstrom, M. a. (2004). Motor-unit coherence and its relation with synchrony are influenced by training. *Journal of Neurophysiology*, 92(6), 3320–3331.
- Sessle, B. J., Adachi, K., Avivi-Arber, L., Lee, J., Nishiura, H., Yao, D., & Yoshino, K. (2007). Neuroplasticity of face primary motor cortex control of orofacial movements. *Archives of Oral Biology*, 52(4), 334–337.
- Sessle, B. J., Yao, D., Nishiura, H., Yoshino, K., Lee, J.-C., Martin, R. E., & Murray, G. M. (2005). Properties and plasticity of the primate somatosensory and motor cortex related to orofacial sensorimotor function. *Clinical and Experimental Pharmacology & Physiology*, 32(1-2), 109–114. Oxford: Blackwell Scientific Publications, 1974-.
- Shaker, R., Dodds, W. J., Dantas, R. O., Hogan, W. J., & Arndorfer, R. C. (1990). Coordination of deglutitive glottic closure with oropharyngeal swallowing. *Gastroenterology*, 98(6), 1478–1484.
- Shaker, R., Dua, K. S., Ren, J., Xie, P., Funahashi, A., & Schapira, R. M. (2002). Vocal cord closure pressure during volitional swallow and other voluntary tasks. *Dysphagia*, 17(1), 13–18.
- Shaker, R., Easterling, C., Kern, M. K., Nitschke, T., Massey, B., Daniels, S. K., Grande, B., et al. (2002). Rehabilitation of swallowing by exercise in tube-fed patients with pharyngeal dysphagia secondary to abnormal UES opening. *Gastroenterology*, 122(5), 1314–1321.
- Shaker, R., Kern, M. K., Bardan, E., Taylor, A., Stewart, E. T., Hoffmann, R. G., Arndorfer, R. C., et al. (1997). Augmentation of deglutitive upper esophageal sphincter opening in the elderly by exercise. *The American Journal of Physiology*, 272(6), G1518–1522.
- Shaker, R., Ren, J., Podvrsan, B., Dodds, W. J., Hogan, W. J., Kern, M. K., Hoffmann, R., et al. (1993). Effect of aging and bolus variables on pharyngeal and upper esophageal sphincter motor function. *The American Journal of Physiology*, 264(3 Pt 1), G427–432.
- El Sharkawi, A., Ramig, L., Logemann, J. A., Pauloski, B. R., Rademaker, A. W., Smith, C. H., Pawlas, A., et al. (2002). Swallowing and voice effects of Lee Silverman Voice Treatment (LSVT): a pilot study. *Journal of Neurology, Neurosurgery, and Psychiatry*, 72(1), 31–36. BMJ Publishing Group Ltd.
- Shaw, J. (1981). Dysphagia in the adult: its clinical significance, diagnosis and management. *The British Journal of Clinical Practice*, 35(1), 13–15.
- Shawker, T. H., Sonies, B. C., & Stone, M. (1984). Soft tissue anatomy of the tongue and floor of the mouth: an ultrasound demonstration. *Brain and Language*, 21(2), 335–350.
- Shibamoto, I., Tanaka, T., Fujishima, I., Katagiri, N., & Uematsu, H. (2007). Cortical activation during solid bolus swallowing. *Journal of Medical and Dental Sciences*, 54(1), 25–30.
- Shinohara, M., & Søgaard, K. (2006). Mechanomyography for studying force fluctuations and muscle fatigue. *Exercise and Sport Sciences Reviews*, 34(2), 59–64.
- Silva, S., Basser, P. J., & Miranda, P. C. (2008). Elucidating the mechanisms and loci of neuronal excitation by transcranial magnetic stimulation using a finite element model of a cortical sulcus. *Clinical Neurophysiology*, 119(10), 2405–2413.

- Singh, S., & Hamdy, S. (2006). Dysphagia in stroke patients. *Postgraduate Medical Journal*, 82(968), 383–391.
- Sohn, Y. H., Jung, H. Y., Kaelin-Lang, A., & Hallett, M. (2003). Excitability of the ipsilateral motor cortex during phasic voluntary hand movement. *Experimental Brain Research*, 148(2), 176–185.
- Soler, E. P., & Ruiz, V. C. (2010). Epidemiology and risk factors of cerebral ischemia and ischemic heart diseases: similarities and differences. *Current Cardiology Reviews*, 6(3), 138–149.
- Sonies, B. C. (1992). Oropharyngeal dysphagia in the elderly. *Clinics in Geriatric Medicine*, 8(3), 569–577.
- Sonies, B. C., Gottlieb, J., Solomon, K., Matthews, B., & Huckabee, M. L. (1997). Simultaneous ultrasound and EMG study of swallowing. *Dysphagia*, 12, 106.
- Sonies, B. C., Wang, C., & Sapper, D. J. (1996). Evaluation of normal and abnormal hyoid bone movement during swallowing by use of ultrasound duplex-Doppler imaging. *Ultrasound in Medicine & Biology*, 22(9), 1169–1175.
- Sowman, P. F., Flavel, S. C., McShane, C. L., Sakuma, S., Miles, T. S., & Nordstrom, M. A. (2009). Asymmetric activation of motor cortex controlling human anterior digastric muscles during speech and target-directed jaw movements. *Journal of Neurophysiology*, 102(1), 159–166.
- Standring, S. (2005). *Gray's anatomy: the anatomical basis of clinical practice* (39th ed.). Elsevier Churchill Livingstone.
- Starmer, H. M., Best, S. R., Agrawal, Y., Chien, W. W., Hillel, A. T., Francis, H. W., Tamargo, R. J., et al. (2012). Prevalence, characteristics, and management of swallowing disorders following cerebellopontine angle surgery. *Otolaryngology Head and Neck Surgery*, 146(3), 419–425.
- Staudenmann, D., Roeleveld, K., Stegeman, D. F., & van Dieën, J. H. (2010). Methodological aspects of SEMG recordings for force estimation—a tutorial and review. *Journal of Electromyography and Kinesiology*, 20(3), 375–387. Elsevier Ltd.
- Steele, C. M., Bailey, G. L., Chau, T., Molfenter, S. M., Oshalla, M., Waito, A. A., & Zoratto, D. C. B. H. (2011). The relationship between hyoid and laryngeal displacement and swallowing impairment. *Clinical Otolaryngology*, 36(1), 30–36. Wiley Online Library.
- Steele, C. M., & Huckabee, M. L. (2007). The influence of orolingual pressure on the timing of pharyngeal pressure events. *Dysphagia*, 22(1), 30–36.
- Steeves, J. D., Zariffa, J., & Kramer, J. L. K. (2011). Are you “tilting at windmills” or undertaking a valid clinical trial? *Yonsei Medical Journal*, 52(5), 701–716.
- Stevens-Lapsley, J., Kluger, B. M., & Schenkman, M. L. (2012). Quadriceps muscle weakness, activation deficits, and fatigue with Parkinson disease. *Neurorehabilitation and Neural Repair*, 26(5), 533–541.

- Stone, M., & Davis, E. P. (1995). A head and transducer support system for making ultrasound images of tongue/jaw movement. *The Journal of the Acoustical Society of America*, 98(6), 3107–3112.
- Suzuki, M., Asada, Y., Ito, J., Hayashi, K., Inoue, H., & Kitano, H. (2003). Activation of cerebellum and basal ganglia on volitional swallowing detected by functional magnetic resonance imaging. *Dysphagia*, 18(2), 71–77.
- Suzuki, T., Connor, N. P., Lee, K., Bless, D. M., Ford, C. N., & Inagi, K. (2002). Age-related alterations in myosin heavy chain isoforms in rat intrinsic laryngeal muscles. *The Annals of Otolaryngology, Rhinology, and Laryngology*, 111(11), 962–967.
- Svensson, P., Romaniello, A., Arendt-Nielsen, L., & Sessle, B. J. (2003). Plasticity in corticomotor control of the human tongue musculature induced by tongue-task training. *Experimental Brain Research*, 152(1), 42–51.
- Svensson, P., Romaniello, A., Wang, K., Arendt-Nielsen, L., & Sessle, B. J. (2006). One hour of tongue-task training is associated with plasticity in corticomotor control of the human tongue musculature. *Experimental Brain Research*, 173(1), 165–173.
- Swinnen, S. P., Schmidt, R. A., Nicholson, D. E., & Shapiro, D. C. (1990). Information feedback for skill acquisition: Instantaneous knowledge of results degrades learning. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 16(4), 706–716.
- Söder, N., & Miller, N. (2002). Using ultrasound to investigate intrapersonal variability in durational aspects of tongue movement during swallowing. *Dysphagia*, 17(4), 288–297.
- Tamura, F., Kikutani, T., Tohara, T., Yoshida, M., & Yaegaki, K. (2012). Tongue thickness relates to nutritional status in the elderly. *Dysphagia*.
- Tanji, J., & Shima, K. (1996). Contrast of neuronal activity between the supplemental motor area and other cortical motor areas. *Advances in Neurology*, 70, 95–103.
- Tassinari, L. G., & Cacioppo, J. T. (2000). The skeletomotor system surface electromyography. In J. T. Cacioppo, L. G. Tassinari, & G. G. Berntson (Eds.), *Handbook of psychophysiology* (2nd ed.). New York: Cambridge University Press.
- Taylor, J. L., & Gandevia, S. C. (2001). Transcranial magnetic stimulation and human muscle fatigue. *Muscle & Nerve*, 24(1), 18–29.
- Teasell, R. W., Foley, N., Fisher, J., & Finestone, H. M. (2002). The incidence, management, and complications of dysphagia in patients with medullary strokes admitted to a rehabilitation unit. *Dysphagia*, 17(2), 115–120.
- Tecchio, F., Zappasodi, F., Pasqualetti, P., De Gennaro, L., Pellicciari, M. C., Ercolani, M., Squitti, R., et al. (2008). Age dependence of primary motor cortex plasticity induced by paired associative stimulation. *Clinical Neurophysiology*, 119(3), 675–682.
- Teismann, I. K., Dziawas, R., Steinstraeter, O., & Pantev, C. (2009). Time-dependent hemispheric shift of the cortical control of volitional swallowing. *Human Brain Mapping*, 30(1), 92–100.

- Teismann, I. K., Suntrup, S., Warnecke, T., Steinsträter, O., Fischer, M., Flöel, A., Ringelstein, E. B., et al. (2011). Cortical swallowing processing in early subacute stroke. *BMC Neurology*, 11(1), 34. BioMed Central Ltd.
- Terk, A. R., Leder, S. B., & Burrell, M. I. (2007). Hyoid bone and laryngeal movement dependent upon presence of a tracheotomy tube. *Dysphagia*, 22(2), 89–93.
- Thexton, A. J., Crompton, A. W., & German, R. Z. (2007). Electromyographic activity during the reflex pharyngeal swallow in the pig: Doty and Bosma (1956) revisited. *Journal of Applied Physiology*, 102(2), 587–600.
- Thomas, C. E., Mayer, S. A., Gungor, Y., Swarup, R., Webster, E. A., Chang, I., Brannagan, T. H., et al. (1997). Myasthenic crisis: clinical features, mortality, complications, and risk factors for prolonged intubation. *Neurology*, 48(5), 1253–1260.
- Thomas, F. J., & Wiles, C. M. (1999). Dysphagia and nutritional status in multiple sclerosis. *Journal of Neurology*, 246(8), 677–682.
- Thompson, S. M., Mattison, H. A., & Nestor, M. W. (2005). Morphological correlates of long-term potentiation and depression. *Cellsciencecom*, 2(2), 1–19.
- Tobimatsu, S., Sun, S. J., Fukui, R., & Kato, M. (1998). Effects of sex, height and age on motor evoked potentials with magnetic stimulation. *Journal of Neurology*, 245(5), 256–261.
- Toogood, J. A., Barr, A. M., Stevens, T. K., Gati, J. S., Menon, R. S., & Martin, R. E. (2005). Discrete functional contributions of cerebral cortical foci in voluntary swallowing: a functional magnetic resonance imaging (fMRI) “Go, No-Go” study. *Experimental Brain Research*, 161(1), 81–90.
- Touge, T., Gerschlagar, W., Brown, P., & Rothwell, J. C. (2001). Are the after-effects of low-frequency rTMS on motor cortex excitability due to changes in the efficacy of cortical synapses? *Clinical Neurophysiology*, 112(11), 2138–2145.
- Tracy, B. L., Ivey, F. M., Hurlbut, D., Martel, G. F., Lemmer, J. T., Siegel, E. L., Metter, E. J., et al. (1999). Muscle quality. II. Effects Of strength training in 65- to 75-yr-old men and women. *Journal of Applied Physiology*, 86(1), 195–201.
- Tracy, J. F., Logemann, J. A., Kahrilas, P. J., Jacob, P., Kobara, M., & Krugler, C. (1989). Preliminary observations on the effects of age on oropharyngeal deglutition. *Dysphagia*, 4(2), 90–94.
- Traurig, H. H. (2008). The Brain Stem and Cranial Nerves. In P. M. Conn (Ed.), *Neuroscience in medicine* (pp. 247–269). Totowa NJ: Humana Press.
- Traversa, R., Cicinelli, P., Oliveri, M., Giuseppina Palmieri, M., Filippi, M. M., Pasqualetti, P., & Rossini, P. M. (2000). Neurophysiological follow-up of motor cortical output in stroke patients. *Clinical Neurophysiology*, 111(9), 1695–1703.
- Troche, M. S., Okun, M. S., Rosenbek, J. C., Musson, N., Fernandez, H. H., Rodriguez, R., Romrell, J., et al. (2010). Aspiration and swallowing in Parkinson disease and rehabilitation with EMST: a randomized trial. *Neurology*, 75(21), 1912–1919.

- Ungerleider, L. G., Doyon, J., & Karni, A. (2002). Imaging brain plasticity during motor skill learning. *Neurobiology of Learning and Memory*, 78(3), 553–564.
- Vaiman, M., Eviatar, E., & Segal, S. (2004). Surface electromyographic studies of swallowing in normal subjects: a review of 440 adults. Report 2. Quantitative data: amplitude measures. *Otolaryngology-Head and Neck Surgery*, 131(5), 773–780.
- Veis, S. L., & Logemann, J. A. (1985). Swallowing disorders in persons with cerebrovascular accident. *Archives of Physical Medicine and Rehabilitation*, 66(6), 372–375.
- Volonte, M., Porta, M., & Comi, G. (2002). Clinical assessment of dysphagia in early phases of Parkinson's disease. *Neurological Sciences*, 23, 121–122. Springer.
- Wagner, T., Valero-Cabre, A., & Pascual-Leone, A. (2007). Noninvasive human brain stimulation. *Annual Review of Biomedical Engineering*, 9, 527–565.
- Walker, F. O. (2004). Neuromuscular ultrasound. *Neurologic Clinics*, 22(3), 563–590, vi.
- Walker, F. O. (2007). Huntington's disease. *Lancet*, 369(9557), 218–228.
- Walker, H. K. (1990). Cranial nerve V: the trigeminal nerve. In H. K. Walker, W. Hall, & J. Hurst (Eds.), *Clinical Methods: The history, physical, and laboratory examinations* (3rd Ed., pp. 318–321). Boston: Butterworths.
- Walker, R. W., Dunn, J. R., & Gray, W. K. (2011). Self-reported dysphagia and its correlates within a prevalent population of people with Parkinson's disease. *Dysphagia*, 26(1), 92–96.
- Walsh, V., & Pascual-Leone, A. (2003). *Transcranial Magnetic Stimulation A Neurochronometrics of Mind*. London: The MIT Press.
- Wang, T.-G., Chang, Y.-C., Chen, W.-S., Lin, P.-H., & Hsiao, T.-Y. (2010). Reduction in hyoid bone forward movement in irradiated nasopharyngeal carcinoma patients with dysphagia. *Archives of physical medicine and rehabilitation*, 91(6), 926–31.
- Warabi, T., Ito, T., Kato, M., Takei, H., Kobayashi, N., & Chiba, S. (2008). Effects of stroke-induced damage to swallow-related areas in the brain on swallowing mechanics of elderly patients. *Geriatrics & Gerontology International*, 8(4), 234–242.
- Ward, N. S. (2006). Compensatory mechanisms in the aging motor system. *Ageing Research Reviews*, 5(3), 239–254.
- Ward, N. S., Brown, M. M., Thompson, A. J., & Frackowiak, R. S. J. (2003). Neural correlates of motor recovery after stroke: a longitudinal fMRI study. *Brain*, 126(11), 2476–2496.
- Wassermann, E. M. (1998). Risk and safety of repetitive transcranial magnetic stimulation: report and suggested guidelines from the International Workshop on the Safety of Repetitive Transcranial Magnetic Stimulation, June 5-7, 1996. *Electroencephalography and Clinical Neurophysiology*, 108(1), 1–16.
- Wassermann, E. M., Epstein, C. M., & Ziemann, U. (2008). *The Oxford handbook of transcranial stimulation*. New York: Oxford Univ Press.

- Wassermann, E. M., Wang, B., Zeffiro, T. A., Sadato, N., Pascual-Leone, A., Toro, C., & Hallett, M. (1996). Locating the motor cortex on the MRI with transcranial magnetic stimulation and PET. *NeuroImage*, 3(1), 1–9.
- Watanabe, Y., Abe, S., Ishikawa, T., Yamada, Y., & Yamane, G. (2004). Cortical regulation during the early stage of initiation of voluntary swallowing in humans. *Dysphagia*, 19(2), 100–108.
- Watkin, K. L., Diouf, I., Gallagher, T. M., Logemann, J. A., Rademaker, A. W., & Ettema, S. L. (2001). Ultrasonic quantification of geniohyoid cross-sectional area and tissue composition: a preliminary study of age and radiation effects. *Head & Neck*, 23(6), 467–474.
- Welle, S., Totterman, S., & Thornton, C. (1996). Effect of age on muscle hypertrophy induced by resistance training. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 51(6), M270–275.
- Wheeler-Hegland, K. M., Ashford, J., Frymark, T., McCabe, D., Mullen, R., Musson, N., Hammond, C. S., et al. (2009). Evidence-based systematic review: Oropharyngeal dysphagia behavioral treatments. Part II-impact of dysphagia treatment on normal swallow function. *Journal of Rehabilitation Research and Development*, 46(2), 185–194.
- Wheeler-Hegland, K. M., Chiara, T., & Sapienza, C. M. (2007). Surface electromyographic activity of the submental muscles during swallow and expiratory pressure threshold training tasks. *Dysphagia*, 22(2), 108–116.
- Wheeler-Hegland, K. M., Rosenbek, J. C., & Sapienza, C. M. (2008). Submental sEMG and hyoid movement during Mendelsohn maneuver, effortful swallow, and expiratory muscle strength training. *Journal of Speech, Language, and Hearing Research*, 51(5), 1072–1087.
- Whyte, J., Gordon, W., & Rothi, L. J. G. (2009). A phased developmental approach to neurorehabilitation research: the science of knowledge building. *Archives of Physical Medicine and Rehabilitation*, 90(11), S3–10. Elsevier Inc.
- Wilkins, T., Gillies, R. A., Thomas, A. M., & Wagner, P. J. (2007). The prevalence of dysphagia in primary care patients: a HamesNet Research Network study. *Journal of the American Board of Family Medicine*, 20(2), 144–150.
- Williamson, D. L., Gallagher, P. M., Carroll, C. C., Raue, U., & Trappe, S. W. (2001). Reduction in hybrid single muscle fiber proportions with resistance training in humans. *Journal of Applied Physiology*, 91(5), 1955–1961.
- Winters-Stone, K. M., & Snow, C. M. (2003). Musculoskeletal response to exercise is greatest in women with low initial values. *Medicine and Science in Sports and Exercise*, 35(10), 1691–1696.
- Wintzen, A. R., Badrising, U. A., Roos, R. A., Vielvoye, J., & Liauw, L. (1994). Influence of bolus volume on hyoid movements in normal individuals and patients with Parkinson's disease. *The Canadian Journal of Neurological Sciences*, 21(1), 57–59.
- Wintzen, A. R., Badrising, U. A., Roos, R. A., Vielvoye, J., Liauw, L., & Pauwels, E. K. (1994). Dysphagia in ambulant patients with Parkinson's disease: common, not dangerous. *The Canadian Journal of Neurological Sciences*, 21(1), 53–56.

- Withers, G. S., & Greenough, W. T. (1989). Reach training selectively alters dendritic branching in subpopulations of layer II-III pyramids in rat motor-somatosensory forelimb cortex. *Neuropsychologia*, 27(1), 61–69.
- Witte, U., Huckabee, M. L., Doeltgen, S. H., Gumbley, F., & Robb, M. (2008). The effect of effortful swallow on pharyngeal manometric measurements during saliva and water swallowing in healthy participants. *Archives of Physical Medicine and Rehabilitation*, 89(5), 822–828.
- Woods, J. J., & Bigland-Ritchie, B. (1983). Linear and non-linear surface EMG/force relationships in human muscles. An anatomical/functional argument for the existence of both. *American Journal of Physical Medicine*, 62(6), 287–299.
- World Health Organization. (1975). Guidelines for evaluation of drugs for use in man. Report of a WHO scientific group. *World Health Organization technical report series*, (563), 1–59.
- Yabunaka, K., Sanada, H., Sanada, S., Konishi, H., Hashimoto, T., Yatake, H., Yamamoto, K., et al. (2011). Sonographic assessment of hyoid bone movement during swallowing: a study of normal adults with advancing age. *Radiological Physics and Technology*, 4(1), 73–77.
- Yao, W., Fuglevand, R. J., & Eoka, R. M. (2000). Motor-unit synchronization increases EMG amplitude and decreases force steadiness of simulated contractions. *Journal of Neurophysiology*, 83(1), 441–452.
- Yarnold, J., & Brotons, M.-C. V. (2010). Pathogenetic mechanisms in radiation fibrosis. *Radiotherapy and Oncology*, 97(1), 149–161.
- Yokoyama, M., Mitomi, N., Tetsuka, K., Tayama, N., & Niimi, S. (2000). Role of laryngeal movement and effect of aging on swallowing pressure in the pharynx and upper esophageal sphincter. *The Laryngoscope*, 110(3), 434–439.
- Yoshida, M., Groher, M. E., Crary, M. A., Mann, G. D. C., & Akagawa, Y. (2007). Comparison of surface electromyographic (sEMG) activity of submental muscles between the head lift and tongue press exercises as a therapeutic exercise for pharyngeal dysphagia. *Gerodontology*, 24(2), 111–116.
- Youmans, S. R., Youmans, G. L., & Stierwalt, J. a G. (2009). Differences in tongue strength across age and gender: is there a diminished strength reserve? *Dysphagia*, 24(1), 57–65.
- Zald, D. H., & Pardo, J. V. (1999). The functional neuroanatomy of voluntary swallowing. *Annals of Neurology*, 46(3), 281–286. Wiley Online Library.
- Zangen, A., Roth, Y., Voller, B., & Hallett, M. (2005). Transcranial magnetic stimulation of deep brain regions: evidence for efficacy of the H-coil. *Clinical Neurophysiology*, 116(4), 775–779.
- Zarahn, E., Rakitin, B., Abela, D., Flynn, J., & Stern, Y. (2007). Age-related changes in brain activation during a delayed item recognition task. *Neurobiology of Aging*, 28(5), 784–798.
- Zhou, S. (2000). Chronic neural adaptations to unilateral exercise: mechanisms of cross education. *Exercise and Sport Sciences Reviews*, 28(4), 177–184.

- Ziemann, U. (2003). Transcranial magnetic stimulation. In M. Hallett (Ed.), *Handbook of Clinical Neurophysiology* (pp. 95–125). New York: Elsevier B.V.
- Ziemann, U., Ilić, T. V., Ilić, T. V., Pauli, C., Meintzschel, F., & Ruge, D. (2004). Learning modifies subsequent induction of long-term potentiation-like and long-term depression-like plasticity in human motor cortex. *The Journal of Neuroscience*, 24(7), 1666–1672.
- Ziemann, U., & Rothwell, J. C. (2000). I-waves in motor cortex. *Journal of Clinical Neurophysiology*, 17(4), 397–405.
- Ziemann, U., Tergau, F., Wassermann, E. M., Wischer, S., Hildebrandt, J., & Paulus, W. (1998). Demonstration of facilitatory I wave interaction in the human motor cortex by paired transcranial magnetic stimulation. *The Journal of Physiology*, 511(1), 181–190.
- Zijdewind, I., Toering, S. T., Bessem, B., Van Der Laan, O., & Diercks, R. L. (2003). Effects of imagery motor training on torque production of ankle plantar flexor muscles. *Muscle & Nerve*, 28(2), 168–173.
- Zoghi, M., Pearce, S. L., & Nordstrom, M. a. (2003). Differential modulation of intracortical inhibition in human motor cortex during selective activation of an intrinsic hand muscle. *The Journal of Physiology*, 550(Pt 3), 933–946.
- Zuydam, A. C., Rogers, S. N., Brown, J. S., Vaughan, E. D., & Magennis, P. (2000). Swallowing rehabilitation after oro-pharyngeal resection for squamous cell carcinoma. *The British Journal of Oral & Maxillofacial Surgery*, 38(5), 513–518.
- Zöllig, J., & Eschen, A. (2009). Measuring compensation and its plasticity across the lifespan. *Restorative Neurology and Neuroscience*, 27(5), 421–433.
- Z'Graggen, W. J., Humm, A. M., Durisch, N., Magistris, M. R., & Rösler, K. M. (2005). Repetitive spinal motor neuron discharges following single transcranial magnetic stimuli: a quantitative study. *Clinical Neurophysiology*, 116(7), 1628–1637.

APPENDICES

Appendix 1: Information sheet – 2-week training protocol

INFORMATION SHEET

Research Title:

Skill Versus Strength Training in Swallowing Rehabilitation

Primary Researcher:

Oshrat Sella , BA

PhD candidate, Department of Communication Disorders

University of Canterbury

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart St., Christchurch NZ

(03) 3786 069

Principal Investigator:

Maggie-Lee Huckabee, PhD

Senior lecturer, Department of Communication Disorders

University of Canterbury

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart St., Christchurch NZ

(03) 378 6070

Co-Investigator:

Richard Jones, BE(Hons), ME, PhD, FACPSEM, FIPENZ, SMIEEE, FAIMBE

Biomedical Engineer & Neuroscientist, Department of Medical Physics and Bioengineering, Canterbury District Health Board.

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart St., Christchurch NZ

(03) 3786 077

Interpreter:

If you need an interpreter, this can be provided

Introduction and aims of the project:

You are invited to participate in a research project that will explore how swallowing training influences the muscles and function of the brain controlling swallowing. This research is a part of a PhD qualification for the lead investigator. Interest in participating should be expressed within 4 weeks of the information being provided. You have the right not to participate in the study or subsequently withdraw from this study at any time.

The aim of this project is to provide important information about the influence of two training techniques on swallowing using different measurements procedures to clarify the relationship between the muscles that are involved in swallowing and the brain control of them, and to understand if one technique is better than the other. Understanding how these techniques influence both nerves and muscles in the swallowing process can improve treatment approaches for swallowing impairment resulting from various brain disorders (e.g., stroke, traumatic brain injury, Parkinson's disease).

Participant selection:

Your participation in this study is due to your reply to advertisements or information seminars requesting research participants. You will complete a questionnaire that will determine your suitability for the study and, if you are a suitable participant for the study, you will be asked to fill in a consent form. The study will include 40 participants who have no swallowing problems. This study will require 20 hours of your time over a period of 2 weeks and 2 days.

Exclusion criteria:

You may not be eligible to participate in this study if you have or ever have had any of the following conditions:

- Stroke
- Swallowing difficulties
- Head and/or neck injury
- Head/ and/or neck surgery
- Any brain-related condition or any illness that caused brain injury
- Neurological disorders (e.g. Multiple Sclerosis etc.)
- Gastroesophageal Reflux Disease

- Family history of epilepsy
- Long standing history of poorly controlled seizures
- Muscular disease (e.g., Muscular atrophy)
- Metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork
- Implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines
- Frequent or severe headaches
- Currently pregnant

The research procedure:

The study involves treatment and assessment sessions at the Van der Veer Institute for Parkinson's and Brain Research.

If you agree to participate in the study, the following steps will occur:

1. You will be given an appointment and asked to come to the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute, 66 Stewart St, Christchurch, New Zealand.
2. A researcher will meet with you at the Van der Veer Institute and you will have an opportunity to have any questions answered. After completing a questionnaire to ensure inclusion criteria are met and risks are minimised you will be asked to sign the consent form. You will then be seated in a comfortable chair and be ready to begin the first assessment session.

Assessment sessions:

3. The first assessment session (before the training) will be preferably held on a Friday, or on a Thursday, and will take 3 hours.

Weight measurements:

4. At the beginning of the assessment session your weight measurements will be recorded to make sure that the ultrasound measurements of your swallowing muscles can be adjusted for your weight.

I. Electromyography measurements

5. Electromyography measures will be taken. Electromyography is used to measure your muscle activity during swallowing. The researcher will attach 2 small electrodes to

the skin underneath your chin, and 1 electrode to your cheek bone. These electrodes are used only for recording and do not put any electricity into the muscles.

6. You will be given a demonstration and directions about how to perform an effortful swallow, which requires you to swallow hard using all the muscles in your mouth and throat.

7. The researcher will attach 2 small electrodes to the skin underneath your chin, and 1 over your cheek bone. These will be used to measure muscle activity when you swallow. These electrodes are used only for recording and do not put any electricity into the muscles.

8. Once the electrodes are in place, you will be asked to complete 5 repetitions of 4 different types of swallows: saliva swallows, 5-ml water swallows, effortful saliva swallows and effortful 5-ml water swallows. This is so the strength of your swallowing can be determined.

II. Manometry measurements

9. Manometry measures will be taken. This procedure measures the pressure in the throat. A small tube will be carefully inserted through one side of your nose. This tube is about the size of a piece of spaghetti and is very soft and flexible. As soon as the tube reaches the back of your throat, you will be required to look up to the ceiling briefly while the tube turns the corner into your upper throat. You can then bring your head back down and will then be handed a glass of water and asked to continuously and comfortably drink the water through a straw. In doing so, the tube will be swallowed into the upper oesophagus

10. The tube will then be slowly pulled upwards until correct placement is assured in the throat. Once in the correct place, a small piece of first aid tape will be wrapped around the tube and secured on your nose to ensure the tube does not move while you swallow.

11. Imbedded in the tube are three discs that measure pressure in the throat. The picture below illustrates how the tube will be inserted through the nose and positioned once it is in the correct place.



12. You will be asked to complete 5 repetitions of 4 different types of swallows: saliva swallows, 5-ml water swallows, effortful saliva swallows and effortful 5-ml water swallows.
13. The tube will then be removed and you will be ready for the next assessment procedure.

III. Ultrasound measurements

14. Ultrasound measurements will be taken. Ultrasound is non-invasive procedure that allows us to measure the size of your swallowing muscles and to visualize how they work during swallowing.
15. You will be seated in a comfortable chair in an examination room at Hagley Radiology (this is located on the ground level of the Van der Veer Institute Building). A head stabilizing unit with two arms will be placed in front of you. One arm will stabilize the imaging tool and one arm will stabilize your head. This stabilizing unit will ensure the measurement are more accurate.
16. You will be asked to bite soft putty in order to have an impression of your teeth so the exact same head position will be maintained during the assessment. The putty will be shaped in a U curve. It will be placed on a U shape plastic mould that will be inserted into the arm on the head stabilizing unit. You will be asked to bite into the putty during the ultrasound procedure in order to remain still.
17. Jelly will be put on the skin under your chin to allow imaging of the muscles. The ultrasound's imaging tool will be lightly placed under your chin by adjusting the stabilizing unit (described above).
18. You will be asked to remain still during the first part of the ultrasound imaging procedure while 2 images of the muscles under your chin will be taken. For the second part you will be asked to complete 5 repetitions of 4 different types of swallows: saliva swallows, 5-ml water swallows, effortful saliva swallows and effortful 5-ml water swallows. During these procedures, you will not feel anything unusual or experience any discomfort.

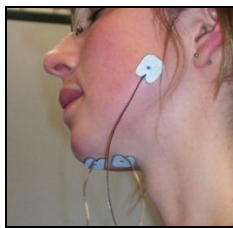
IV. Motor Evoked Potentials (MEPs)

19. MEPs will be assessed using a technique called transcranial magnetic stimulation (TMS). Your brain will be stimulated using TMS which consists of a figure-of-eight coil that is held over your scalp (see picture 2). When you contract the muscles used for swallowing, the electrical activity in these muscles will trigger this coil to stimulate your brain using a magnetic pulse. This will feel like someone is tapping you on the head but will not hurt. You may also feel a small twitch in the arm opposite the side of the brain being stimulated. When the magnetic pulse is triggered, your brain sends an electric

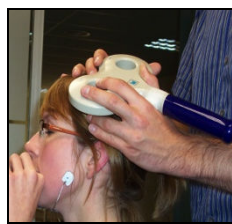
signal to your swallowing muscles, which is measured using the electrodes placed under your chin. This signal is called a motor evoked potential or MEP (see picture 3).

20. The researcher will attach two small electrodes to the skin underneath your chin, and one over your cheek bone (see picture 1). These will be used to measure muscle activity when you swallow. These electrodes are used only for recording and do not put any electricity into the muscles.

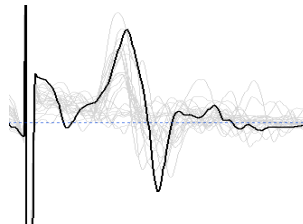
21. Once the electrodes are in place, you will be asked to swallow your saliva 10 times and contract the muscles under your chin as hard as you can 10 times. This is so the strength of your swallows can be determined and will enable the researchers to adjust the equipment to your individual muscle activity during swallowing.



Picture 1



Picture 2



Picture 3

22. In the second assessment session we will identify which areas of the brain are activated by the magnetic stimulation and how to best apply that stimulation. Starting on the left side of your head, and then moving to the right, several steps need to be taken.

a. First, the best area for stimulating brain signals (MEPs) will be identified by measuring MEPs from several places on your scalp and finding which place gives the best response. The researcher will use the magnetic stimulator to find the place on your skull which creates the biggest swallowing signal. During this time you will feel a twitch in the muscles under your chin and a sensation of ‘tapping’ on your head. Once this area has been determined, the position of the coil will be marked on the scalp using a non-permanent pen.

b. Next, we will evaluate how strong the magnetic pulse needs to be to stimulate your brain and what level is best for doing the research. Starting with a very soft ‘tap’, or magnetic pulse, we will slowly increase the intensity until we determine the lowest level of stimulation required. Then we will increase the intensity until the swallowing signals do not get any larger.

c. These steps will be completed on both sides of your head. This will help the researchers identify which side of your brain is involved more in controlling the muscles used for swallowing. All further MEP measurements will be made at the identified location on that side of your brain.

23. Once the area described above has been identified, the researchers will measure MEPs during 15 saliva swallows and 15 repetitions of contracting the muscles under your chin in order to compare measurements done after you have completed the training.

V. Training sessions

24. Once your first (baseline) assessment session is completed, you will be scheduled for 10 training sessions starting on a Monday. The training sessions will be held every weekday (Monday-Friday) for two weeks. Each session will last for one hour. The type of training will vary depending on which training group you are assigned to:

a. *Strength training:* You will have two electrodes placed under your chin and one over your jaw bone. These electrodes will record the activity of your muscles under the chin. You will be seated in front of a computer screen. The electrodes will give you feedback about the strength of your swallowing. You will then be instructed to swallow your saliva normally. For the next swallow, you will be asked to “swallow hard with all the muscles in your mouth and throat”. You will receive visual feedback and encouraged to swallow harder so an increase in muscle strength is seen. Each session will be divided to 5 sections, each 10 minutes long, with a 2.5 minutes break between each section. If you will need a longer break you will receive it.

b. *Skill training:* As with the other task, you will have two electrodes placed under your chin and one over your jaw bone. These electrodes will record the activity of your muscles under the chin. You will be seated in front of a computer screen. The electrodes will give you feedback about the precision of your swallows. You will need to swallow accurately enough to ‘hit’ a target on the screen. You will receive visual feedback about how precise you were. Each session will be divided to 5 sections, each 10 minutes long, with a 2.5 minutes break between each section. If you will need a longer break you will receive it.

VI. Additional assessments:

25. After the first training session and after the last (10th) training session the researcher will assess your MEPs using TMS (described in step 19). The researcher will repeat steps 20-21. Step 23 will be repeated 5 min, 30 min, 60 min and 90 min after the end of the training. The aim of this procedure is to assess the immediate effects of the training.

VII. Outcome measurements

26. The last assessment session will be held on a Monday following completion of your 2-week training programme at the Van der Veer Institute.

27. In the last assessment session the researcher will repeat the same assessment done on the first session: weight (described in step 4), electromyography (described in steps 5-8), manometry (described in steps 9-13), ultrasound (described in steps 14-18) and MEP (described in steps 19-21, 23).

28. The whole research project should take approximately 12 lab sessions over a period of two weeks plus two days. 20 hours in total.

Below is a table summarising training and assessments time:

<i>Base line assessment</i>	<i>First training session + MEPs assessment</i>	<i>Training sessions: 2nd-9th</i>	<i>Last (10th) training session + MEPs assessment</i>	<i>Outcome assessment</i>
Thursday / Friday	Monday	Week 1: Tuesday-Friday Week 2: Monday-Thursday	Friday	Tuesday
Ultrasound Manometry sEMG	MEPs Procedure A Training MEPs- Procedure B	Training	Training MEPs- Procedure B	MEPs Procedure A Ultrasound Manometry sEMG
2 hours	4-5 hours (2 hr + 1 hr + 2 hrs)	8 hours (8 sessions*1 hr each)	3 hours (1 hr + 2 hrs)	2.5 hours

Risks and Benefits:

Single-pulse TMS, as applied in this study, is considered to carry no risk beyond occasionally causing local discomfort at the site of stimulation and headaches that last for a short while in subjects who are prone to headache. Completing the exclusion criterion questionnaire will ensure any risks are identified and minimized.

You will not gain any direct benefits as an individual although you will receive vouchers worth \$150 as reimbursement for travel expenses. In addition during the first assessment session, last assessment session, and the first and last training session you will be offered a light meal. You will be part of a study that contributes important information on how swallowing training influences the muscles that control swallowing and will clarify how the brain activity changes due to training. This information will assist with the development of improved treatment techniques for swallowing disorders.

Though not expected, you will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. The Van der Veer Institute has equipment for dealing with medical emergencies.

Participation:

If you agree to take part in this study, you are free to withdraw at any time, without having to give a reason.

Confidentiality:

Research findings will be presented at international research meetings and submitted for publication in peer reviewed journals. Additionally, research findings will be made available to the local Canterbury medical community through research presentations and regional forums. However, no material which could personally identify you will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked Swallowing Research Laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of ten years after data collection is complete, at which time they will be destroyed. With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee

Atypical findings:

You will be notified about any atypical findings that might be revealed during the assessments, and upon your consent we will this information to your GP.

Results:

If requested, you will be offered copies of the publications that arise from this research. However, you should be aware that a significant delay may occur between completion of data collection and completion of the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the lead investigator.

Questions:

You may have a friend, family, or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require.

Please contact the primary researcher, Oshrat Sella, if you require any further information about the study. Oshrat can be contacted during work hours at 03-3786069 or after hours at 021-2576793. Email: oshrat.sella@vanderveer.org.nz

If you have any queries or concerns about your rights as a participant in this study, you may wish to contact a Health and Disability Advocate, telephone:

South Island 0800 377 766 or 03-3777501 in Christchurch. Free Fax (NZ wide): 0800 2787 7678 (08002SUPPORT) Email (NZ wide): advocacy@hdc.org.nz

This study has received ethical approval from the Upper South A Regional Ethics Committee.

Appendix 2: Questionnaire

QUESTIONNAIRE

Skill vs. Strength in Swallowing Rehabilitation

Identifying number: _____ Age: _____ D.O.B: _____

Which ethnic group(s) do you belong to?

- | | |
|---|--|
| <input type="checkbox"/> New Zealand European | <input type="checkbox"/> New Zealand Maori |
| <input type="checkbox"/> Samoan | <input type="checkbox"/> Cook Island Maori |
| <input type="checkbox"/> Tongan | <input type="checkbox"/> Niuean |
| <input type="checkbox"/> Chinese | <input type="checkbox"/> Indian |
| <input type="checkbox"/> Other _____ | |

Please complete the following questionnaire by ticking the box that is most applicable to you.

Do you suffer from the effects of any of the following medical problems?:

- ☐ Stroke
- ☐ Swallowing difficulties
- ☐ Head and/or neck injury
- ☐ Head/ and/or neck surgery
- ☐ Any brain-related condition or any illness that caused brain injury
- ☐ Neurological disorders (e.g. Multiple Sclerosis etc.)
- ☐ Gastroesophageal Reflux Disease
- ☐ Family history of epilepsy
- ☐ Long standing history of poorly controlled seizures
- ☐ Muscular disease (e.g., Muscular atrophy)
- ☐ Metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork
- ☐ Implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines
- ☐ Frequent or severe headaches
- ☐ Currently pregnant

Do you have any other medical problems, which you feel may impact on your ability to participate? Yes / No (Please circle one)

If **yes**, please describe: _____

Are you currently taking any medications that may affect your swallowing? Yes / No (Please circle one)

If **yes**, please describe _____

Appendix 3: Consent form – 2-week training protocol

CONSENT FORM Skill vs. Strength Training in Swallowing Rehabilitation

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Oute mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai

I, _____, have read and I understand the Information Sheet dated _____ for volunteers taking part in the study designed to compare two rehabilitation treatments for swallowing disorders. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given. I have had this project explained to me by _____.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my current, continuing or future health care. I understand that if I choose to withdraw from the study, I may also withdraw all information that I have provided.

I understand that the information obtained from this research may be published. However, I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

I understand that the investigation will be stopped if it should appear harmful to me and I know who to contact if I have any side effects to the study or have any questions about the study.

I understand the potential risks of participation in the study as explained to me by the researcher.

I understand the compensation provisions for this study.

I have had time to consider whether to take part.

I wish to receive a copy of the results: YES / NO

I wish to be notified of any atypical findings that might be revealed during the assessments: YES / NO

After being advised of such, I wish to have any atypical findings reported to my GP: YES / NO

I, _____ hereby consent to take part in this study.

Date _____ Signature _____

Signature of researcher _____ Name of researcher _____

Name of primary researcher and contact phone number: Oshrat Sella 03-3786069

Appendix 4: Information sheet – 4-week training protocol

INFORMATION SHEET

Research Title:

Skill Versus Strength Training in Swallowing Rehabilitation: Evaluation of Dose Effects

Primary Researcher:

Oshrat Sella , BA

PhD candidate, Department of Communication Disorders

University of Canterbury

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart St., Christchurch NZ

(03) 3786 069

Principal Investigator:

Maggie-Lee Huckabee, PhD

Senior lecturer, Department of Communication Disorders

University of Canterbury

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart St., Christchurch NZ

(03) 378 6070

Co-Investigator:

Richard Jones, BE(Hons), ME, PhD

Biomedical Engineer & Neuroscientist, Department of Medical Physics and Bioengineering,
Canterbury District Health Board.

Van der Veer Institute for Parkinson's and Brain Research

66 Stewart St., Christchurch NZ

(03) 3786 077

Interpreter:

If you need an interpreter, this can be provided

Introduction and aims of the project:

You are invited to participate in an extension to the research project that you currently are enrolled in that will explore how the dose of swallowing training influences the muscles and function of the brain controlling swallowing. You are invited to participate in the study only if you are currently completing the study entitled “Skill Versus Strength Training in Swallowing Rehabilitation”. This research is a part of a PhD qualification for the lead investigator. Interest in participating should be expressed within 1 week of the information being provided. You have the right not to participate in the study or subsequently withdraw from this study at any time.

This project is an extension of the project you are already participating in. The aim of the overall project is to provide important information about the influence of two training techniques on swallowing using different measurements procedures, to clarify the relationship between the muscles that are involved in swallowing and the brain control of them, and to understand if one technique is better than the other. This extension of the study aims to extend the findings of the first study by evaluating the effects of an extended dose of training. Understanding how these techniques influence both nerves and muscles in the swallowing process can improve treatment approaches for swallowing impairment resulting from various brain disorders (e.g., stroke, traumatic brain injury, Parkinson’s disease).

Participant selection:

You are invited to participate in the study only if you are currently completing the current study entitled 'Skill Versus Strength Training in Swallowing Rehabilitation'. The study will include 20 participants from the original group. This study will require another 12.5 hours of your time over a period of two weeks plus 1 day.

The research procedure:

The extended study involves 8 training session and 2 assessment sessions at the Van der Veer Institute for Parkinson’s and Brain Research.

If you agree to participate in the study, the following steps will occur:

1. You will be asked to sign an additional consent form.
2. You will continue with the primary study you are involved in.
3. Upon completion of the final assessment for the primary study, you will continue with your swallowing training. The additional training will begin the day following the final outcome sessions for the first project. The additional training will be composed of 8 sessions of the same type of training you are currently doing.

Assessment sessions:

4. You will undergo two assessment sessions. (a) One will be conducted right after the 18th training session. It will be held on a Friday and will take 2 hours in addition to 1 hour of training (b) The second assessment session is an outcome session and will take 2.5 hours.

(a) After the last (18th) training session the researcher will assess the communication between your brain and muscles by stimulating your brain and measuring the signal in the muscle during two tasks. This is done exactly as it was done in the first study. This test will be repeated 5 min, 30 min, 60 min and 90 min after the end of the training. The aim of this procedure is to assess the immediate effects of the training.

(b) The final outcome session will be held on the Tuesday of the week following the completion of the training. In this outcome session the researcher will repeat the same assessments done on the outcome session that follows the completion of the 10 training sessions. We will again measure electrical activity in muscles, pressure and movement of structures in the throat during swallowing and muscle size. We can provide you with another information sheet from the first study which explains these tests in detail at your request.

5. This additional study will take additional 9 lab sessions over a period of two weeks plus one day, 12.5 hours in total.

The whole research project (the original study plus this additional study) will take approximately 21 lab sessions over a period of four weeks plus two days, 34 hours in total.

Risks and Benefits:

Single-pulse TMS, as applied in this study, is considered to carry no risk beyond occasionally causing local discomfort at the site of stimulation and headaches that last for a short while in subjects who are prone to headache. Completing the exclusion criterion questionnaire will ensure any risks are identified and minimized.

You will not gain any direct benefits as an individual although you will receive additional vouchers worth \$100 as reimbursement for travel expenses. In addition, you will be offered a light meal during the 4-weeks assessment session, and during the 18th training session. You will be part of a study that contributes important information on how swallowing training influences the muscles that control swallowing and will clarify how the brain activity changes due to training.

This information will assist with the development of improved treatment techniques for swallowing disorders.

Though not expected, you will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. The Van der Veer Institute has equipment for dealing with medical emergencies.

Participation:

If you agree to take part in this study, you are free to withdraw at any time, without having to give a reason.

Confidentiality:

Research findings will be presented at international research meetings and submitted for publication in peer reviewed journals. Additionally, research findings will be made available to the local Canterbury medical community through research presentations and regional forums. However, no material, which could personally identify you, will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked Swallowing Research Laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of ten years after data collection is complete, at which time they will be destroyed. With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee

Atypical findings:

You will be notified about any atypical findings that might be revealed during the assessment and, with your consent, send a copy of this information to your GP.

Results:

If interested, you will be offered copies of the publications that arise from this research. However, please be aware that a significant delay may occur between completion of data collection and completion of the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the lead investigator.

Questions:

You may have a friend, family, or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require.

Please contact the primary researcher, Oshrat Sella, if you require any further information about the study.

Oshrat can be contacted during work hours at 03-3786069 or after hours at 021-2576793.

Email: oshrat.sella@vanderveer.org.nz

If you have any queries or concerns about your rights as a participant in this study, you may wish to contact a Health and Disability Advocate, telephone:

South Island 0800 377 766 or 03-3777501 in Christchurch. Free Fax (NZ wide): 0800 2787 7678 (08002SUPPORT) Email (NZ wide): advocacy@hdc.org.nz

This study has received ethical approval from the Upper South A Regional Ethics Committee.

Appendix 5: Consent form – 4-week training protocol

<p style="text-align: center;">CONSENT FORM</p> <p style="text-align: center;">Skill vs. Strength Training in Swallowing Rehabilitation:</p> <p style="text-align: center;">Evaluation of Dose Effects</p>

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Oute mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai

I, _____, have read and I understand the Information Sheet dated _____ for volunteers taking part in the study designed to compare two rehabilitation treatments for swallowing disorders. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given. I have had this project explained to me by _____.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my current, continuing or future health care. I understand that if I choose to withdraw from the study, I may also withdraw all information that I have provided.

I understand that the information obtained from this research may be published. However, I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

I understand that the investigation will be stopped if it should appear harmful to me and I know who to contact if I have any side effects to the study or have any questions about the study.

I understand the potential risks of participation in the study as explained to me by the researcher.

I understand the compensation provisions for this study.

I have had time to consider whether to take part.

I wish to receive a copy of the results: YES / NO

I wish to be notified of any atypical findings that might be revealed during the assessments: YES / NO

After being advised of such, I wish to have any atypical findings reported to my GP: YES / NO

I, _____ hereby consent to take part in this study.

Date _____ Signature _____

Signature of researcher _____ Name of researcher _____

Name of primary researcher and contact phone number: Oshrat Sella 03-3786069

Appendix 6: Swallowing training questionnaire

		Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
1	My training was interesting	1	2	3	4	5
2	My training was boring	1	2	3	4	5
3	I enjoyed my training	1	2	3	4	5
4	I disliked my training	1	2	3	4	5
5	I feel that my swallowing improved during the training	1	2	3	4	5
6	I feel that my swallowing deteriorated during the training	1	2	3	4	5
7	I feel the training made my swallowing muscles stronger	1	2	3	4	5
8	I feel the training made my swallowing muscles weaker	1	2	3	4	5
9	I feel that the training made my swallowing more accurate	1	2	3	4	5
10	I experienced pain during my training*	1	2	3	4	5

*If you experienced pain during the training, please elaborate: _____

If you have any further comments regarding ANY aspect of your swallowing training, please write them here: _____

Appendix 7: Raw data – manometry – 4-week training

Raw data for peak pressure in all three sensors (1-3) during all four tasks: effortful saliva, effortful water swallowing, non-effortful saliva, and non-effortful water swallowing, at baseline, post 2-week training, and post 4-week training

Four-week training protocol - Manometry data: Peak amplitude (mmHg) of sensors 1, 2 & 3 at baseline, post 2 weeks & post 4 weeks, during effortful saliva swallowing. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2-week training, C post 4-week training

Subject ID	S1 A	S1 B	S1 C	S2 A	S2 B	S2 C	S3 A	S3 B	S3 C
SKL-D 73 M	151.1	143.1	124.8	164.3	82.3	120.8	-11.2	-14.7	-23.4
SKL-D 88 F	75.5	156.9	131.7	134.4	47.4	61.7	1.0	-4.1	0.3
SKL-I 21 F	114.9	163.1	146.0	119.1	130.6	176.9	-2.0	-6.8	-15.6
SKL-I 29 M	161.5	162.9	156.9	150.9	199.4	173.1	-17.8	1.8	-12.6
SKL-I 67 M	66.5	80.5	64.5	247.0	222.5	132.7	-6.0	-2.3	-13.7
SKL-I 85 M	71.3	70.9	134.5	79.2	136.1	176.6	-14.4	-19.5	-13.0
STR 22 F	110.1	130.5	132.2	151.3	198.0	228.3	-11.9	-11.5	-8.1
STR 35 F	163.4	127.6	122.9	97.2	90.3	75.4	-17.2	-30.5	-23.2
STR 67 F	159.3	144.7	129.4	114.7	106.8	200.9	4.6	5.7	-0.2

Four-week training protocol - Manometry data: Peak amplitude (mmHg) of sensors 1, 2 & 3 at baseline, post 2 weeks & post 4 weeks, during effortful 10 mL water swallowing. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2- week training, C post 4-week training

Subject ID	S1 A	S1 B	S1 C	S2 A	S2 B	S2 C	S3 A	S3 B	S3 C
SKL-D 73 M	140.8	145.7	154.9	183.1	136.7	110.4	-7.5	-3.4	-4.5
SKL-D 88 F	67.0	195.0	117.9	101.3	50.1	57.7	1.8	2.8	-4.1
SKL-I 21 F	103.4	105.3	84.8	109.5	105.7	96.4	-2.4	-7.8	-10.4
SKL-I 29 M	160.6	157.9	193.6	97.7	167.0	132.5	-3.2	8.9	-10.1
SKL-I 67 M	67.1	80.1	75.5	264.7	259.7	110.6	-0.9	-2.3	-21.8
SKL-I 85 M	66.7	77.7	102.5	87.8	130.9	231.5	-0.8	-17.2	-9.7
STR 22 F	113.6	122.0	120.3	140.9	171.0	155.7	-10.1	-8.0	-1.2
STR 35 F	168.3	148.5	149.1	103.3	101.3	87.4	-16.5	-19.3	-24.7
STR 67 F	95.3	84.1	80.3	142.7	136.7	143.0	8.3	3.2	5.0

Four-week training protocol - Manometry data: Peak amplitude (mmHg) of sensors 1, 2 & 3 at baseline, post 2 weeks & post 4 weeks, during non-effortful saliva swallowing. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2-week training, C post 4-week training

ID	S1 A	S1 B	S1 C	S2 A	S2 B	S2 C	S3 A	S3 B	S3 C
SKL-D 73 M	131.9	125.2	87.8	122.8	84.3	92.0	-19.3	-15.6	-15.9
SKL-D 88 F	73.9	158.6	140.9	109.4	56.8	52.4	-2.6	2.1	-3.4
SKL-I 21 F	115.1	127.5	123.4	104.1	113.0	73.7	-10.1	-13.0	-2.8
SKL-I 29 M	166.0	142.2	128.1	114.5	144.1	174.0	-4.9	-4.4	-19.8
SKL-I 67 M	78.1	82.7	102.8	65.3	124.1	107.4	-8.5	-1.2	-15.4
SKL-I 85 M	69.4	74.4	102.0	66.8	63.3	90.6	-9.7	-11.7	-5.8
STR 22 F	112.6	102.2	109.2	133.8	127.9	129.0	-11.8	-10.3	-13.6
STR 35 F	170.0	103.0	112.3	110.2	84.8	94.0	-14.5	-19.1	-18.0
STR 67 F	85.1	84.5	74.7	181.8	234.2	107.5	-3.7	-4.3	-0.1

Four-week training protocol - Manometry data: Peak amplitude (mmHg) of sensors 1, 2 & 3 at baseline, post 2 weeks & post 4 weeks, during non-effortful 10 mL water swallowing. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2-week training, C post 4-week training (n.a – missing data)

Subject ID	S1 A	S1 B	S1 C	S2 A	S2 B	S2 C	S3 A	S3 B	S3 C
SKL-D 73 M	125.4	138.8	124.6	158.6	66.8	71.8	-1.8	-9.5	-6.6
SKL-D 88 F	65.6	147.4	130.6	130.4	57.0	59.7	1.6	3.4	-6.2
SKL-I 21 F	62.5	86.3	62.2	89.0	91.2	92.3	-4.8	-14.2	-11.9
SKL-I 29 M	121.3	138.5	141.2	81.9	147.8	106.0	n.a	n.a	-24.9
SKL-I 67 M	71.7	79.4	124.5	54.1	208.5	66.3	-3.0	1.0	-5.2
SKL-I 85 M	69.6	80.1	74.3	72.3	97.1	168.3	-5.6	-13.4	-6.1
STR 22 F	104.9	110.2	104.6	112.3	141.0	111.4	-6.0	-11.0	-5.4
STR 35 F	109.6	112.5	128.5	95.4	87.9	90.3	-7.2	-24.6	-16.0
STR 67 F	25.6	33.6	43.8	226.7	219.2	205.0	0.1	1.4	2.4

Raw data for duration of pressure in all three sensors (1-3) during all four tasks: effortful saliva, effortful water swallowing, non-effortful saliva, and non-effortful water swallowing, at baseline, post 2-weeks training, and post 4-weeks training

Four-week training protocol - Manometry data: Duration (s) of sensors 1, 2 & 3 at baseline, post 2 weeks & post 4 weeks, during effortful saliva swallowing. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2- week training, C post 4-week training

Subject ID	S1 A	S1 B	S1 C	S2 A	S2 B	S2 C	S3 A	S3 B	S3 C
SKL-D 73 M	0.743	0.534	0.735	0.449	0.657	0.574	1.754	1.926	1.374
SKL-D 88 F	0.518	0.422	0.331	0.266	0.446	0.424	1.173	1.214	1.546
SKL-I 21 F	0.550	0.564	0.548	0.534	0.477	0.469	1.074	0.787	0.985
SKL-I 29 M	0.474	0.620	0.655	0.261	0.564	0.718	0.968	0.645	0.786
SKL-I 67 M	0.968	0.838	0.855	0.878	0.830	0.789	1.269	1.055	1.774
SKL-I 85 M	0.564	0.605	0.467	0.735	0.935	1.358	1.338	1.696	1.930
STR 22 F	0.546	0.748	0.844	0.462	0.834	0.822	1.136	1.495	1.008
STR 35 F	0.340	0.339	0.583	0.262	0.410	0.498	1.797	1.706	1.799
STR 67 F	1.722	1.361	1.866	1.700	1.386	1.974	1.302	1.227	2.227

Four-week training protocol - Manometry data: Duration (s) of sensors 1, 2 & 3 at baseline, post 2 weeks & post 4 weeks, during effortful 10 mL swallowing. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2-week training, C post 4-week training

Subject ID	S1 A	S1 B	S1 C	S2 A	S2 B	S2 C	S3 A	S3 B	S3 C
SKL-D 73 M	0.506	0.754	0.658	0.456	0.614	0.601	2.226	1.866	1.603
SKL-D 88 F	0.470	0.442	0.303	0.301	0.560	0.382	0.922	1.284	1.335
SKL-I 21 F	0.476	0.514	0.510	0.446	0.539	0.575	1.034	1.189	1.372
SKL-I 29 M	0.371	0.404	0.407	0.154	0.242	0.226	0.768	0.593	0.862
SKL-I 67 M	0.738	0.794	0.586	0.551	0.707	0.486	1.078	1.093	1.651
SKL-I 85 M	0.420	0.392	0.405	0.478	0.591	0.624	1.336	1.314	1.685
STR 22 F	0.482	0.641	0.718	0.362	0.666	0.755	1.294	1.653	1.426
STR 35 F	0.326	0.378	0.351	0.386	0.223	0.369	1.779	1.674	1.761
STR 67 F	0.666	1.264	1.407	0.622	1.340	1.316	1.557	1.423	1.766

*Four-week training protocol - Manometry data: Duration (s) of sensors 1, 2 & 3 at baseline, post 2 weeks & post 4 weeks, during **non-effortful saliva swallowing**. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2-week training, C post 4-week training*

Subject ID	S1 A	S1 B	S1 C	S2 A	S2 B	S2 C	S3 A	S3 B	S3 C
SKL-D 73 M	0.675	0.475	0.540	0.438	0.591	0.418	0.863	1.503	0.902
SKL-D 88 F	0.366	0.323	0.275	0.208	0.336	0.398	1.002	1.216	1.317
SKL-I 21 F	0.462	0.452	0.447	0.425	0.435	0.460	1.033	1.059	1.124
SKL-I 29 M	0.439	0.439	0.448	0.377	0.298	0.328	0.799	0.639	0.779
SKL-I 67 M	0.694	0.773	0.592	0.401	0.584	0.450	0.944	1.003	1.626
SKL-I 85 M	0.492	0.456	0.461	0.452	0.780	1.138	1.069	1.660	1.755
STR 22 F	0.510	0.498	0.500	0.378	0.379	0.409	1.263	1.559	1.483
STR 35 F	0.339	0.287	0.354	0.211	0.181	0.207	1.705	1.311	1.332
STR 67 F	0.443	0.507	0.474	0.338	0.301	0.307	1.095	1.107	0.853

*Four-week training protocol - Manometry data: Duration (s) of sensors 1, 2 & 3 at baseline, post 2 weeks & post 4 weeks, during **non-effortful 10 mL swallowing**. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2-weeks training, C post 4-week training (n.a. – missing data)*

Subject ID	S1 A	S1 B	S1 C	S2 A	S2 B	S2 C	S3 A	S3 B	S3 C
SKL-D 73 M	0.533	0.424	0.521	0.362	0.610	0.362	1.178	1.861	1.324
SKL-D 88 F	0.342	0.250	0.272	0.199	0.326	0.412	0.943	1.169	1.363
SKL-I 21 F	0.364	0.378	0.288	0.356	0.408	0.412	1.057	1.315	1.240
SKL-I 29 M	0.261	0.405	0.255	0.170	0.228	0.171	n.a.	n.a.	0.922
SKL-I 67 M	0.435	0.599	0.426	0.219	0.385	0.310	0.995	0.925	1.500
SKL-I 85 M	0.300	0.348	0.382	0.322	0.454	0.999	1.057	1.442	1.786
STR 22 F	0.324	0.466	0.394	0.240	0.396	0.308	1.587	1.655	1.746
STR 35 F	0.222	0.249	0.230	0.193	0.193	0.164	1.684	1.250	1.537
STR 67 F	0.239	0.290	0.281	0.251	0.262	0.238	1.297	1.190	1.058

Raw data for relative durations (pharyngeal pressure timing measurements) during all four tasks: effortful saliva, effortful water swallowing, non-effortful saliva, and non-effortful water swallowing, at baseline, post 2-week training, and post 4-week training

Four-week training protocol - Manometry data: Relative duration (s) at baseline, post 2 weeks & post 4 weeks, during effortful saliva swallowing. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2-week training, C post 4-week training. S1-S2 time duration between peak of sensor 1 to peak of sensor 2, S1-S3 time duration between onset of sensor 1 to onset of sensor 3

Subject ID	S1-S2 A	S1-S2 B	S1-S2 C	S1-S3 A	S1-S3 B	S1-S3 C
SKL-D 73 M	0.206	0.358	0.222	-0.866	-0.922	-0.439
SKL-D 88 F	0.351	0.378	0.309	-0.189	-0.405	-0.551
SKL-I 21 F	0.162	0.079	0.131	-0.191	0.073	-0.094
SKL-I 29 M	0.282	0.096	0.154	-0.060	0.081	0.174
SKL-I 67 M	0.267	0.196	0.427	-0.046	-0.063	-0.108
SKL-I 85 M	0.246	0.354	0.269	-0.119	-0.217	-0.374
STR 22 F	0.288	0.089	0.027	-0.174	-0.178	-0.145
STR 35 F	0.338	0.312	0.432	-0.737	-0.646	-0.478
STR 67 F	0.082	0.071	0.138	-0.143	-0.009	-0.076

Four-week training protocol - Manometry data: Relative duration (s) at baseline, post 2 weeks & post 4 weeks, during effortful 10 mL water swallowing. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2week training, C post 4-week training. S1-S2 time duration between peak of sensor 1 to peak of sensor 2, S1-S3 time duration between onset of sensor 1 to onset of sensor 3

Subject ID	S1-S2 A	S1-S2 B	S1-S2 C	S1-S3 A	S1-S3 B	S1-S3 C
SKL-D 73 M	0.173	0.303	0.295	-1.534	-0.419	-0.390
SKL-D 88 F	0.340	0.390	0.326	-0.215	-0.272	-0.446
SKL-I 21 F	0.106	0.112	0.222	-0.330	-0.276	-0.318
SKL-I 29 M	0.254	0.176	0.217	-0.066	0.128	-0.180
SKL-I 67 M	0.185	0.174	0.465	-0.145	-0.182	-0.351
SKL-I 85 M	0.234	0.214	0.410	-0.336	-0.386	-0.450
STR 22 F	0.314	0.037	0.063	-0.347	-0.442	-0.280
STR 35 F	0.345	0.353	0.349	-0.700	-0.582	-0.654
STR 67 F	0.134	0.087	0.113	-0.366	-0.222	-0.124

*Four-week training protocol - Manometry data: Relative duration (s) at baseline, post 2 weeks & post 4 weeks, during **non-effortful saliva swallowing**. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2-week training, C post 4-week training. S1-S2 time duration between peak of sensor 1 to peak of sensor 2, S1-S3 time duration between onset of sensor 1 to onset of sensor 3*

Subject ID	S1-S2 A	S1-S2 B	S1-S2 C	S1-S3 A	S1-S3 B	S1-S3 C
SKL-D 73 M	0.130	0.331	0.180	-0.097	-0.371	-0.212
SKL-D 88 F	0.232	0.333	0.291	-0.217	-0.393	-0.394
SKL-I 21 F	0.250	0.234	0.224	-0.093	-0.146	-0.131
SKL-I 29 M	0.157	0.116	0.152	-0.014	-0.028	-0.073
SKL-I 67 M	0.379	0.268	0.352	-0.077	-0.075	-0.284
SKL-I 85 M	0.250	0.213	0.291	-0.147	-0.191	-0.084
STR 22 F	0.402	0.298	0.290	-0.185	-0.110	-0.138
STR 35 F	0.304	0.261	0.23	-0.627	-0.435	-0.588
STR 67 F	0.216	0.323	0.147	-0.144	-0.181	-0.081

*Four-week training protocol - Manometry data: Relative duration (s) at baseline, post 2 weeks & post 4 weeks, during **non-effortful 10 mL water swallowing**. S1 sensor 1 at upper pharynx, S2 sensor 2 at mid-pharynx, S3 sensor 3 at UES; A baseline, B post 2- week training, C post 4-week training. S1-S2 time duration between peak of sensor 1 to peak of sensor 2, S1-S3 time duration between onset of sensor 1 to onset of sensor 3(n.a. – missing data)*

Subject ID	S1-S2 A	S1-S2 B	S1-S2 C	S1-S3 A	S1-S3 B	S1-S3 C
SKL-D 73 M	0.170	0.235	0.250	-0.630	-0.840	-0.564
SKL-D 88 F	0.260	0.310	0.277	-0.270	-0.342	-0.438
SKL-I 21 F	0.201	0.209	0.226	-0.258	-0.325	-0.327
SKL-I 29 M	0.198	0.150	0.166	n.a.	n.a.	-0.337
SKL-I 67 M	0.334	0.221	0.260	-0.286	-0.246	-0.391
SKL-I 85 M	0.184	0.218	0.230	-0.389	-0.389	-0.393
STR 22 F	0.324	0.317	0.250	-0.328	-0.378	-0.265
STR 35 F	0.202	0.242	0.230	-0.655	-0.587	-0.721
STR 67 F	0.215	0.232	0.220	-0.414	-0.364	-0.373

Appendix 8: Raw data – submental activation – 4-week training

Raw data for activation of the submental muscle group: sEMG peak amplitude - Four-week training protocol

Mean of sEMG peak amplitude (μV) at baseline, post 2 weeks and post 4 weeks of training, during effortful saliva swallowing task, for each participant in the 4 weeks protocol

	Effortful saliva	Effortful saliva	Effortful saliva
ID	Baseline	Post 2 weeks	Post 4 weeks
SKL-D 53 F	160.3	121.5	68.1
SKL-D 73 M	58.8	89.0	95.0
SKL-D 88 F	105.7	134.7	96.8
SKL-I 21 F	43.8	130.2	146.1
SKL-I 29 M	240.2	172.6	142.8
SKL-I 67 M	197.6	188.2	207.0
SKL-I 85 M	132.9	128.5	102.9
STR 22 F	150.9	315.7	548.1
STR 35 F	253.8	230.2	n.a.
STR 67 F	128.9	150.1	119.4

Mean of sEMG peak amplitude (μV) at baseline, post 2 weeks and post 4 weeks of training, during effortful 10 mL water swallowing task for each participant in the 4 weeks protocol

	10ml Effort	10ml Effort Post	10ml Effort Post
ID	Baseline	2 weeks	4 weeks
SKL-D 53 F	170.5	133.5	81.3
SKL-D 73 M	60.70	89.1	80.9
SKL-D 88 F	99.6	111.6	72.1
SKL-I 21 F	65.4	125.5	119.4
SKL-I 29 M	181.4	189.7	183.5
SKL-I 67 M	188.8	114.9	134.3
SKL-I 85 M	147.2	124.0	122.3
STR 22 F	144.8	290.2	518.2

STR 35 F	343.0	310.6	Missing
STR 67 F	38.7	126.1	122.0

Mean of sEMG peak amplitude at baseline, post 2 weeks and post 4 weeks of training, during non-effortful saliva swallowing task, for each participant in the 4 weeks protocol

ID	Non-effortful saliva		
	Baseline	Post 2 weeks	Post 4 weeks
SKL-D 53 F	27.5	31.5	34.9
SKL-D 73 M	46.3	57.7	26.4
SKL-D 88 F	42.6	51.6	51.6
SKL-I 21 F	24.5	46.9	78.3
SKL-I 29 M	43.8	101.2	36.0
SKL-I 67 M	58.7	61.3	74.8
SKL-I 85 M	70.2	51.7	29.8
STR 22 F	87.1	153.7	101.2
STR 35 F	227.1	108.7	142.3
STR 67 F	15.4	17.6	9.9

Mean of sEMG peak amplitude (μV) at baseline, post 2 weeks and post 4 weeks of training, during effortful 10 mL swallowing task for each participant in the 4 weeks protocol

ID	Non-effortful 10 mL		
	Baseline	Post 2 weeks	Post 4 weeks
SKL-D 53 F	34.4	33.2	48.7
SKL-D 73 M	45.2	40.2	27.5
SKL-D 88 F	31.9	35.4	49.9
SKL-I 21 F	21.8	44.6	72.9
SKL-I 29 M	50.7	101.0	41.6
SKL-I 67 M	54.9	40.2	56.3
SKL-I 85 M	59.5	55.8	50.3
STR 22 F	43.2	82.8	56.3
STR 35 F	193.0	172.8	162.9
STR 67 F	15.5	16.6	10.1

Appendix 9: Eating Assessment Tool (EAT-10)

**The University of Canterbury Department of Communication Disorders
Swallowing Rehabilitation Research Laboratory and Clinics
at the Van der Veer Institute**

Some patients with movement disorders have difficulty with chewing and swallowing their food. This self-assessment tool might help you identify if you are experiencing any difficulties in these areas. Please complete the short questionnaire below and return it to the front desk.

**Eating Assessment Tool (EAT-10)
(Belafsky, et al., 2008)**

Circle the appropriate response.

To what extent are the following scenarios problematic for you?	0 = no problem		4 = severe problem		
My swallowing problem has caused me to lose weight.	0	1	2	3	4
My swallowing problem interferes with my ability to go out for meals.	0	1	2	3	4
Swallowing liquids takes extra effort.	0	1	2	3	4
Swallowing solids takes extra effort.	0	1	2	3	4
Swallowing pills takes extra effort.	0	1	2	3	4
Swallowing is painful.	0	1	2	3	4
The pleasure of eating is affected by my swallowing.	0	1	2	3	4
When I swallow food sticks in my throat.	0	1	2	3	4
I cough when I eat.	0	1	2	3	4
Swallowing is stressful.	0	1	2	3	4

Would you like to be contacted by clinicians at the Swallowing Rehabilitation Clinics for an assessment? Please leave your name and telephone number below.

Name: _____

Phone: _____

Appendix 10: Information sheet – PD study

INFORMATION SHEET

Research Title:

Swallowing Skill Therapy in Parkinson's Disease

Primary Researcher:

Oshrat Sella , BA
PhD candidate, Department of Communication Disorders
University of Canterbury
Van der Veer Institute for Parkinson's and Brain Research
66 Stewart St., Christchurch NZ
(03) 3786 069

Principal Investigator:

Maggie-Lee Huckabee, PhD
Senior lecturer, Department of Communication Disorders
University of Canterbury
Van der Veer Institute for Parkinson's and Brain Research
66 Stewart St., Christchurch NZ
(03) 378 6070

Co-Investigator:

Richard Jones, BE(Hons), ME, PhD
Biomedical Engineer & Neuroscientist, Department of Medical Physics and Bioengineering,
Canterbury District Health Board.
Van der Veer Institute for Parkinson's and Brain Research
66 Stewart St., Christchurch NZ
(03) 3786 077

Tim Anderson, BSc(Hons), MBChB, MD, FRACP
Acting Director, Van der Veer Institute
Professor, Department of Medicine, University of Otago, Christchurch
Neurologist, Department of Neurology, Canterbury District Health Board
Van der Veer Institute for Parkinson's and Brain Research

66 Stewart St., Christchurch NZ
(03) 378 6079

Rachel Bennett, honours student in Bachelor of Speech Language Therapy Degree Programme,
University of Canterbury.

Van der Veer Institute for Parkinson's and Brain Research
66 Stewart St., Christchurch NZ
(03) 378 6070

Interpreter:

If you need an interpreter, this can be provided

Introduction and aims of the project:

You are invited to participate in a research project that will explore how swallowing skill therapy influences your swallowing ability and your swallowing muscles. This research is a part of a PhD qualification for the lead investigator. Interest in participating should be expressed within 1 week of the information being provided. You have the right not to participate in the study or subsequently withdraw from this study at any time.

The aim of this project is to provide important information about the influence of a skill training technique on swallowing function using different measurements. Understanding how this technique influence swallowing function and swallowing muscles can improve treatment approaches for swallowing impairment in Parkinson's disease.

Participant selection:

You have been identified as a potential participant for this study based on your recent evaluation of swallowing at the Swallowing Rehabilitation Research Laboratory. After reading this information sheet, you are free to consent to participate in our research project, or you may receive swallowing rehabilitation services through the laboratory that are not a part of the study. Declining to participate in the study will in no way compromise your current or potential future treatment at the Swallowing Rehabilitation Research Laboratory. If you consent to participate in this study, you will be asked to fill in a consent form prior to initiating the treatment.

Inclusion criteria:

You are eligible to participate in this study if you have the following conditions:

- Parkinson`s disease as diagnosed by a neurologist
- Self reported swallowing difficulties that last for at least 2 months

Exclusion criteria:

You may **not** be eligible to participate in this study if you have the following conditions:

- Parkinsonism that is not caused by Parkinson`s disease, for example: Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP), side effects of medications, such as some antipsychotics.
- Dementia
- Stroke
- Head and/or neck injury
- Head/ and/or neck surgery
- Muscular disease (e.g., Muscular atrophy)

The research procedure:

The study involves assessment and therapy sessions at the Van der Veer Institute for Parkinson`s and Brain Research.

If you agree to participate in the study, the following steps will occur:

1. You will be given an appointment and asked to come to the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute, 66 Stewart St, Christchurch, New Zealand.
2. A researcher will meet with you at the Van der Veer Institute and you will have an opportunity to have any questions answered. After completing a questionnaire to ensure inclusion criteria are met, you will be asked to sign the consent form. If you agree to participate in the study, you will also be providing consent to use information collecting during your first swallowing assessment in the research. You will then be seated in a comfortable chair and be ready to begin the first assessment session.

A. ASSESSMENT SESSION (BASELINE)

VIII. Clinical Swallowing Assessment

3. You will undergo a clinical assessment of your swallowing function. This assessment is a standard evaluation procedure performed in our clinic to evaluate the presence of

swallowing difficulties in all patients that are referred to our swallowing clinic. This standard evaluation includes the following:

- a. The nerves that are involved in swallowing are assessed by asking you to make certain movements in the muscles around your mouth, tongue and face.
- b. The clinician will ask you to eat and drink small amounts of food and water. The clinician will document their observation of your eating behaviour; for example, how well you have chewed your food and whether you cough during eating or drinking. If you have any dietary restriction, those will be taken into consideration.
- c. You will be asked to inhale some citric acid using a face mask, and your reaction will be documented. This test will help in understanding how strong your cough is, and how fast you cough.
- d. You will be given a cup filled with 150 ml of tap water and the clinician will measure the time it takes you to drink the water and how many times you swallowed during that time. This test will help in understanding how efficient your swallowing is.

IX. Electromyography (EMG) Measurements

4. Electromyography (EMG) measures will be taken. EMG is used to measure your muscle activity during swallowing. The researcher will attach 3 small discs to the skin underneath your chin. These discs are used to record electrical activity only and do not put any electricity into the muscles.
5. You will be given a demonstration and directions about how to perform an effortful swallow, which requires you to swallow hard using all the muscles in your mouth and throat.
6. Once the electrodes are in place, you will be asked to complete 5 repetitions of 4 different types of swallows: saliva swallows, 10-ml water swallows, effortful saliva swallows and effortful 10-ml water swallows. This is so the strength of your swallowing can be determined.

X. Ultrasound Measurements

7. Ultrasound measurements will be taken. Ultrasound is non-invasive procedure that allows us to measure the size of your swallowing muscles and to visualize how they work during swallowing.
8. You will be seated in a comfortable chair. A head stabilizing unit with two arms will be placed in front of you. One arm will stabilize the imaging tool and one arm will stabilize your head. This stabilizing unit will ensure the measurements are more accurate.

9. You will be asked to bite soft putty in order to have an impression of your teeth so the exact same head position will be maintained during the assessment. The putty will be shaped in a U curve. It will be placed on a U shape plastic mould that will be inserted into the arm on the head stabilizing unit. You will be asked to bite into the putty during the ultrasound procedure in order to remain still.
10. Jelly will be put on the skin under your chin to allow imaging of the muscles. The ultrasound's imaging tool will be lightly placed under your chin by adjusting the stabilizing unit (described above).
11. You will be asked to remain still during the first part of the ultrasound imaging procedure while 5 images of the muscles under your chin will be taken. For the second part you will be asked to complete 5 repetitions of saliva swallows. During these procedures, you will not feel anything unusual or experience any discomfort.

XI. Quality of Life in Swallowing Disorders Questionnaire (SWAL-QOL)

You will be asked to fill in a questionnaire. This questionnaire is designed to find out how your swallowing problem has been affecting your day-to-day quality of life.

B. THERAPY SESSIONS

XII. Swallowing Skill Therapy

12. Once your first (baseline) assessment session is completed, you will be scheduled for 10 training sessions starting on a Monday. The training sessions will be held every weekday (Monday-Friday) for two weeks. Each session will last for one hour.
13. You will have two electrodes (small metal discs) placed under your chin and one over your jaw bone. These electrodes will record the activity of your muscles under the chin and present that information to you in the form of a moving line on the computer. You will be seated in front of a computer screen. The electrodes will give you feedback about the precision of your swallowing movements. You will need to swallow accurately enough so that the waveform created by your swallowing is able to "hit" a target on the screen. You will receive visual feedback about how precise you were. When you swallow with great precision, the target becomes smaller so you have to be even more precise. If you miss the target, it will become bigger. Each session will be divided to 5 sections, each 10 minutes long, with a 2.5 minutes break between each section. If you will need a longer break, you will receive it.

C. OUTCOME SESSIONS

XIII. Outcome measurements

14. Two outcome assessment sessions will be performed: the **first** one will be held on the Monday following completion of your 2-week training programme (3 days after your last training session), and the **second** one will be held 2 weeks following the completion of your training, on a Monday as well. Both outcome sessions will be carried out at the Van der Veer Institute.
15. During the first outcome session and the second outcome session, the researcher will repeat the same assessment done on the first (baseline) session: clinical swallowing assessment (described in step 3), EMG (described in steps 4-6), ultrasound (described in steps 7-11) and filling in SWAL-QOL questionnaire (described in paragraph IV)
16. The whole research project should take approximately 13 lab sessions over a period of four weeks plus two days, 16 hours in total.

Below is a table summarising training and assessments time:

<i>Base-line Assessment</i>	<i>Therapy sessions: 1st-10th</i>	<i>First Outcome Session</i>	<i>Second Outcome Session</i>
Thursday / Friday	Week 1: Monday-Friday Week 2: Monday-Friday	Monday	Monday
Clinical swallowing assessment EMG Ultrasound SWAL-QOL	Skill training	Clinical swallowing assessment EMG Ultrasound SWAL-QOL	Clinical swallowing assessment EMG Ultrasound SWAL-QOL
2 hours	10 hours (10 sessions*1 hr each)	2 hours	2 hours

Risks and Benefits:

You will be part of a study that contributes important information on how swallowing training influences swallowing function. This information will assist with the development of improved treatment techniques for swallowing disorders. It is anticipated that some participants will experience an improvement in swallowing function after the therapy, although this cannot be promised.

Though not expected, you will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. The Van der Veer Institute has equipment for dealing with medical emergencies.

Participation:

If you agree to take part in this study, you are free to withdraw at any time, without having to give a reason.

Confidentiality:

Research findings will be presented at international research meetings and submitted for publication in peer reviewed journals. Additionally, research findings will be made available to the local Canterbury medical community through research presentations and regional forums. However, no material that could personally identify you will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked Swallowing Research Laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of ten years after data collection is complete, at which time they will be destroyed. With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee

Atypical findings:

You will be notified about any atypical findings that might be revealed during the assessments, and upon your consent we will this information to your GP.

Results:

If requested, you will be offered copies of the publications that arise from this research. However, you should be aware that a significant delay may occur between completion of data collection and completion of the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the lead investigator.

Questions:

You may have a friend, family, or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require.

Please contact the primary researcher, Oshrat Sella, if you require any further information about the study. Oshrat can be contacted during work hours at 03-3786069 or after hours at 021-2576793. Email: oshrat.sella@vanderveer.org.nz

If you have any queries or concerns about your rights as a participant in this study, you may wish to contact a Health and Disability Advocate, telephone:

South Island 0800 377 766 or 03-3777501 in Christchurch. Free Fax (NZ wide): 0800 2787 7678 (08002SUPPORT) Email (NZ wide): advocacy@hdc.org.nz

This study has received ethical approval from the Upper South B Regional Ethics Committee.

Appendix 11: Questionnaire – PD study

QUESTIONNAIRE Swallowing Skill Therapy in Parkinson`s Disease

Identifying number: _____ Age: _____ D.O.B: _____

Which ethnic group(s) do you belong to?

- | | |
|---|--|
| <input type="checkbox"/> New Zealand European | <input type="checkbox"/> New Zealand Maori |
| <input type="checkbox"/> Samoan | <input type="checkbox"/> Cook Island Maori |
| <input type="checkbox"/> Tongan | <input type="checkbox"/> Niuean |
| <input type="checkbox"/> Chinese | <input type="checkbox"/> Indian |
| <input type="checkbox"/> Other _____ | |

Please complete the following questionnaire by ticking the box that is most applicable to you.

Do you suffer from the effects of any of the following medical problems?:

- ☐ Stroke
- ☐ Dementia
- ☐ Head and/or neck injury
- ☐ Head and/or neck surgery
- ☐ Neurological disorders other than Parkinson`s disease
- ☐ Gastroesophageal Reflux Disease
- ☐ Muscular disease (e.g., Muscular atrophy)

Do you have any other medical problems which you feel may impact on your ability to participate? Yes / No (Please circle one)

If yes, please describe:

Are you currently taking any medications that may affect your swallowing?

Yes / No (Please circle one)

If yes, please describe

Appendix 12: Consent form – PD study

CONSENT FORM Swallowing Skill Therapy in Parkinson's Disease

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Oute mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai

I, _____, have read and I understand the Information Sheet dated _____ for volunteers taking part in the study designed to explore the effects of swallowing skill therapy among people with Parkinson's disease. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given. I have had this project explained to me by _____.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my current, continuing or future health care. I understand that if I choose to withdraw from the study, I may also withdraw all information that I have provided.

I understand that the information obtained from this research may be published. However, I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

I understand that the investigation will be stopped if it should appear harmful to me and I know who to contact if I have any side effects to the study or have any questions about the study.

I understand the potential risks of participation in the study as explained to me by the researcher.

I understand the compensation provisions for this study.

I have had time to consider whether to take part.

I wish to receive a copy of the results: YES / NO

I wish to be notified of any atypical findings that might be revealed during the assessments: YES / NO

After being advised of such, I wish to have any atypical findings reported to my GP: YES / NO

I, _____ hereby consent to take part in this study.

Date _____ Signature _____

Signature of researcher _____ Name of researcher _____

Name of primary researcher and contact phone numbers: Oshrat Sella 03-3786069

